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## CONTENTS



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# American Journal of Pharmacy

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THE AMERICAN
JOURNAL OF PHARMACY

*DECEMBER, 1918*

## EDITORIAL.

### PROFESSIONALISM AND PHARISAISM.

In the light of recent events, the query is propounded what is professional pharmacy? Accepting the meaning as laid down in the accepted dictionaries:—Pharmacy "is the art or practice of preparing, preserving and compounding medicines, and of dispensing them according to the formulæ or prescriptions of medical practitioners." These authorities commonly elucidate further by stating "the occupation of a druggist" or "the occupation of an apothecary or pharmaceutical chemist." Thus the lexicographers support the synonymous use of the words pharmacist, apothecary and druggist.

Profession is defined in the Century Dictionary as "The calling or occupation which one professes to understand and to follow: vocation, specifically a vocation in which a professed knowledge of some department of science or learning is used by its *practical application* to the affairs of others, either in advising, guiding or teaching them, or in serving their interests or welfare in the practice of the art founded upon it." This standard work further explains: "The word implies professed attainments in special knowledge as distinguished from mere skill, a practical dealing with affairs, as distinguished from mere study or investigation, and an application of such knowledge to uses for others *as a vocation,* as distinguished from its pursuit for one's own purposes."

The acceptance of these definitions would justify the opinion that the practical application, *as a vocation,* of the special knowledge of the art of preparing, preserving, compounding and dispensing, constitutes professional pharmacy. A contingent of extremists, however, would set aside the authority of the lexicographers and adopt a definition for professional pharmacy that would eliminate many

of those who have devotedly served as pharmacists in their respective communities and would restrict pharmaceutical professionalism to those "professional pharmacists who are with our colleges of pharmacy and our pharmaceutical manufacturing houses." By arrogant assumption these would apply the term pharmacist to many who have never devoted either time or study to pharmacy as a vocation and who are actually outside of the etymology of the term professional pharmacy. A supercilious air of superiority has been assumed by some whose limited field of specialized study and lack of experience would not justify placing them in charge of a pharmacy with any expectation that they could successfully discharge the numerous commercial and professional services demanded of the practical pharmacist.

Throughout the entire world's history, society has demanded of the apothecary many services not strictly pharmaceutic and the supplying of many articles besides medicine. This is readily accounted for by the wide range of substances that have been more or less associated wtih the healing art and the store of general knowledge required of the druggist. In the Mosaic records we find the art of the apothecary applied not only in the preparation of the ointments of that day but likewise to the manufacture of confections, incenses and perfumes.

It is admitted that the unethical practice of medicine in this country and the business spirit of the age has led many of our druggists to give more attention to side lines and commercial matters than to the professional duties of their vocation and that some of their stores bear but little resemblance to pharmacies. This is an evil which in time will be corrected by education, well-defined rules for the ethical practice of medicine and pharmacy supported by legislation. This calls for a propaganda of education and rectification but it is not a proper ground for the basing of a wholesale denunciation and condemnation of the pharmacists of the United States and a discrediting of the work of the pharmaceutical schools and journals upon whose conscientious efforts with the coming generations of pharmacists will depend very largely the elimination of such errors of practice. Do any of the other professions indulge in such wholesale denunciation of their members because some engage in unethical and demoralizing practices?

Proper education is a fundamental to the professional status of any vocation and before American pharmacy can be considered as

established upon a scientifically sound professional basis, we must have a law in every state, territory and insular possession that will fix as a prerequisite to the license to practice pharmacy a proper preliminary scholastic attainment followed by a pharmaceutical education in an approved school of pharmacy. Our pharmaceutical associations, both state and national, have been very lax in their duty in not securing this primary essential for the recognition of pharmacy as a profession. As we study the statistics available on this subject, we are confronted by an anomaly, namely, that some of the states that are supporting universities and whose teachers in the department of pharmacy are energetically declaiming professional pharmacy, have no such prerequisite laws. Under these conditions, it is evident that pharmaceutical reform should be initiated at home.

Much has been said of the need for original research and investigation in pharmacy and the writer is heartily in accord with the idea that research is a proper corner stone for our structure of professional pharmacy. However, as we review the situation, we recognize that this limitless field of investigation has not been neglected by American pharmacists; that they have made many valuable contributions and doubtless in the future many more studies worthy of the name of research will demonstrate American ingenuity and ability in this line of work. A review of the literature covering pharmaceutical research, exhibits another anomaly, namely, that many of those who have been so pronouncedly professional in thought and so generous in the advocacy have not been constructive contributors to pharmaceutical research and some of their names do not appear connected with any work worthy of the name of research. There can be no comparison between lip service and scientific accomplishment and the untilled fields awaiting their energies is an undeniable appeal.

The advancement of pharmacy will be by the processes of evolution and not by revolution. The leaven is at work, the internal work is progressing and the education of the public as to the value of pharmacy is proceeding, perhaps too slowly, and requiring further speeding assistance. Let us build the structure, in which we are so vitally interested, on the solid foundation of genuine professional pharmaceutical service and devoid of pharisaism.

G. M. B.

## AN EDITORIAL CAMOUFLAGE.

In the current issue, our esteemed cotemporary the *Northwestern Druggist* publishes an editorial under the caption "Camouflage in Pharmacy." In this the learned editor has painted a disparaging word picture of the practice of pharmacy in the United States. If his portrayal be true, then to say the least, it cannot be considered as at all creditable to the pharmaceutical educators of the country, among whom we include the editor, who have devoted so many years to the teaching of "technical and scientific pharmacy."

That pharmacy as practiced in many drug stores, does not measure up to proper ideals is granted; but is not a similar statement equally true regarding the practice of every profession? In his attempt to discredit commercialism in pharmacy, our editorial friend has permitted his earnestness to lead him into vehement statements and wholesale denunciation which will not withstand deliberate analysis and a comparison with the established facts.

The following extracts are examples of the specious arguments presented:

"In the construction of the U. S. P. IX, the peer of all national pharmacopœias, he has been conspicuous by his absence. Scientific prescription dispensing of a very high order is well known but rarely practiced.

"Our present pharmacopœia has been held up as a criterion of the professional standing and scientific qualifications of the retail druggists of America. This is pure camouflage. On the entire revision committee, which committee is responsible for the U. S. P. IX there are only two retail pharmacists and one is a professor in a college of pharmacy.

"The U. S. P. IX reflects the progress which scientific and professional pharmacy has made during the past fifteen years in this country. It is the work of professional pharmacists who are with our colleges of pharmacy and our pharmaceutical manufacturing houses. It is an indication of the required professional qualifications which the public has a right to expect of those who compound and dispense medicines."

By no means are we willing to admit that "scientific prescription dispensing is rarely practiced." Neither are we as American pharmacists willing to admit that the dispensing in the United States is not as scientific and as exact as in any other country. In an ex-

perience of more than forty years, it has been my good fortune to become acquainted with many practical pharmacists as well as with very many estimable teachers in the schools of pharmacy and these alike have upheld the ethics of the profession and, possessing the requisite knowledge, have taken pride in their ability to compound and dispense medicines in the most skillful and scientific manner. The impression that remains is that there is no town of any size in the United States where scientific prescription dispensing of a very high order is not practiced. Our friend possibly has failed to attend the meetings of the Section on Practical Pharmacy and Dispensing of the American Pharmaceutical Association.

The Pharmacopœia of the United States is admittedly the peer of any national pharmacopœia, but who has made it so? The U. S. P. IX is the product of the improvements and advances incorporated in each of the previous revisions and since the revision of 1840, practical pharmacists have contributed very largely to the revisions. Can our friend be so unacquainted with the history of the various revisions of the pharmacopœia that he fails to give due credit to the work of the practical pharmacists thereon? Many of the formulas, admitted by foreign authorities as being superior to their own, have been originated or improved by practical pharmacists and these have added greatly to the reputation and admitted high standing of our national pharmacopœia.

The statement that there are only two retail pharmacists on the present committee of revision is not correct and further it is very misleading. A reference to the list of the members selected by the Pharmacopœial Convention as the Committee of Revision as published in the preface of the U. S. P. IX,—pages xlii–xliii, will prove this statement to be erroneous. Further, it can be shown that a very large percentage of the committee had a pharmaceutical education and that, at some period, many had been engaged as practical retail pharmacists and no doubt their work in the revision amply reflected the knowledge and experience gained in such professional service. Moreover, in the recent filling of vacancies on this committee, at least three more retail pharmacists were elected.

The pharmacists have certainly no reason to offer apologies for the quantity or the quality of the services they rendered in the revisions of the Pharmacopœia of the United States.

G. M. B.

# BOLSHEVISM IN PHARMACY.[1]

By Charles H. LaWall, Ph.M.

Words and phrases have associated concepts which may differ so greatly in different individuals that when these individuals enter into a discussion they are often talking about things which are diametrically opposed. "Pharmaceutical education," "pharmaceutical practice" and "pharmaceutical progress" are examples of phrases, often the subject of controversy, in which there is no common ground of understanding. Indeed it is often true that these concepts are changed in the individual under the influence of time and environment. No definition of a liberal education has ever been given which surpasses the following, by Huxley, which is quoted to show how comprehensive and detailed a definition sometimes becomes.

"That man, I think, has had a liberal education who has been so trained in youth that his body is the ready servant of his will, and does with ease and pleasure all the work that, as a mechanism, it is capable of; whose intellect is a clear, cold, logic engine, with all its parts of equal strength, and in smooth working order; ready like a steam engine to be turned to any kind of work, and spin the gossamers as well as forge the anchors of the mind; whose mind is stored with a knowledge of the great and fundamental truths of nature and of the laws of her operations; one, who, no stunted ascetic, is full of life and fire, but whose passions are trained to come to heel by a vigorous will, the servant of a tender conscience; who has learned to love all beauty, whether of nature or of art, to hate all vileness, and to respect others as himself."

When we come to the question of pharmaceutical education or any other kind of scientific or professional education, however, we are dealing with a more restricted and specialized field. Without attempting to inflict upon you an arbitrary definition of this kind of education, I will state that I believe *that man is best educated who is most useful to his community and to his profession or trade,* whatever it may be. For further explanation of my personal views on some of these questions, I will take the unusual liberty of referring you to two previous articles in which I have expressed them. One

[1] Read at the November meeting of the Philadelphia Branch of the American Pharmaceutical Association.

is the address of the chairman of the Section on Education and Legislation of the American Pharmaceutical Association, published in the Proceedings for 1910, page 605. The other is an article entitled "When is an Education not an Education?" *Journ. A. Ph. A.*, 1915, p. 176. The views expressed on fundamentals in these two articles have not materially changed during the passage of time, but conditions have recently arisen which seem to call for further expression of opinion on certain phases of the situation.

There seems to be at present, a peculiar tendency to throw discredit on commercialism of any kind in connection with pharmacy. The reason for this is seen every time one looks into the windows or sees the advertisements of a certain type of drug store, but why the large number of high minded, ethical pharmacists, who are practicing their profession with the respect and support of leading members of the medical profession in their communities, should on that account be held up to scorn, is hard to understand.

We are led to believe that because Mr. X. or Mr. Y. makes a larger proportion of his gross profits from the sale of merchandise other than drugs, that pharmacy is going to the dogs. Why should any stigma attach to a man because he is a good merchandiser? This double responsibility of such an individual to the community has been well expressed by Dr. Jacob Diner as follows:

"On one side we must have the professionally trained man; on the other we must prepare the same man to be commercially able to avail himself of every honest, legitimate means for the financial advancement of his business."

The attempt to classify pharmacists according to professional attainments has been recurrent for centuries past. One of the first recorded legal enactments affecting pharmacy was that of Frederic II of Sicily in 1233 A.D. This law mentions "apotheca" in the sense of warehouses where drugs were stored; compounders of medicines were called "confectionarii," and sellers of simple medicines were called "stationarii." As throwing light on the subject of "side lines," the following will be found of interest:

In the sixteenth century the Guild of Nuremburg druggists presented a memorial of grievances in which, among others, are the following complaints:

1. The sale of all confections has now fallen into the hands of the sugar dealer.

2. Counter sales (of spices) are now made by all of the large

spice and cheap corner grocery shops, thus robbing the druggist of a source of profit that he is justly entitled to.

3. The sale of sundries, such as sealing wax, fumigating pastilles, paper, ink and pens, is now taking place in common huckster shops.

4. The sugar dealers are not only selling confections but also all kinds of fruit juices and all such preserves as do not deteriorate in the course of a year.

These same Nuremburg pharmacists stated that "many of our brethren have matriculated at universities, some have attended academies and others have even graduated as doctors. We consider that our profession is not a trade but is in reality a free art."

In the eighteenth century the pharmacists were held in derision for their claim to professional recognition, by Professor Hoffmann, one of the early professors of the University of Halle, who stated their scope of knowledge in the following way:

"The apothecary should know that an acid and an alkali, when brought into contact, will effervesce. It will suffice if he but know the effect although he may be ignorant of the cause."

Business or commercial ability is fundamentally responsible for success in any profession or for the continued existence of educational institutions, even those engaged in the most academic and intellectual lines of work. All rivalry or competition is in reality commercial rivalry or competition, and whether this is carried on fairly or unfairly depends upon the underlying principles of honesty, fair dealing and ethics possessed by the participants.

What are the primary objects of a college education in pharmacy? Is it to produce mental contortionists and star performers who can assimilate syllabi and transform the pabulum into passing marks for registration examinations, or is it to produce worthy, helpful members of the community? If we decide that the latter is preferable, the means must be studied and methods applied which will tend to produce the desired results. I say "tend to," for no idealistic attainment of results will ever be possible. We must work toward a desired end, whether we at first reach it or not.

We must discourage empiricism in scientific work and encourage an interest in and thoroughness of training in principles. Efficiency, success, service, are all factors of value and importance. We must encourage and teach the student to become accurate in his work and in his habits of thought, and if our work is conscientious and thor-

ough, and the student is receptive and interested, we shall have contributed to the community an individual who will be a credit to his work and to his college and who will be a safe and ethical dispenser of extemporaneous medicines, whether they constitute five or fifty per cent. of his gross sales.

A certain number of the members of any group of young men and women have a natural aptitude and a greater liking for scientific work than for general drug store work. These should be given the necessary post graduate instruction to enable them to become the neighborhood analysts and bacteriologists, to act as clinical advisers to the physicians of their communities, and should be trained to be helpful even along the broader lines of sanitation and hygiene, so as to give aid to local health officers when needed. The preliminary education required for the best results should be a minimum of four years of high school work. This requirement should be enacted into the State laws, as has recently been done in the State of Illinois.

Any college of pharmacy with the proper equipment and instructional staff should be able to, and should have the right to teach both of such classes of pharmacists in such numbers as present themselves with properly accredited entrance credentials. That pharmacy is gradually separating into two distinct classes no one will deny. That it has been predicted for years, everybody knows. That it can be brought about over night by resolution, agreement or law, is impossible. Such views savor of Bolshevism, a specious, plausible, irresponsible type of propaganda which has been worrying statesmen for several years, but has not previously appeared in educational discussions.

To accomplish these changes needs more than the fiat of any individual or group of individuals. We cannot effect reform by resolution any more than we can decide scientific questions by a majority vote. Diplomas, degrees and certificates are but "scraps of paper" unless upheld by legislative enactment. Reformers frequently forget that laws are primarily for the protection of the public and not for the development of theories which are impossible to put into practice.

It is in the matter of legislation that we find our greatest stumbling block to rapid progress. Our prerequisite legislation is too recent and not widespread enough as yet, to make such radical changes as would be necessary to effect an immediate sharp separation between drug merchandisers and professional pharmacists, de-

sirable as it may seem in some extreme instances. Economic factors would be ignored, State laws would need to be changed, boards of pharmacy would have to cast aside the traditions and practices of a generation. Dr. Beal has truly said "Compromise is the price of progress," and with this thought in mind, we should take pains to see that legal restrictions and educational qualifications should be coordinated and drawn closer together, not forced apart.

Looking back, therefore, at the whole subject, it is clear to my mind that any educational institution should be proud of the opportunity of training both pharmacists and druggists, if by druggists is meant the large number of self-sacrificing individuals who, during the recent influenza epidemic, closed everything but their prescription departments so as to devote their entire attention to the pharmaceutical needs of the communities in which they practiced.

The object of an education is that a man may learn to benefit himself by serving others, one who exemplifies the words applied by our own Dean Remington to a noble deceased pharmacist:

> "A man whose soul is pure and strong,
> Whose sword is bright and keen;
> Who knows the splendor of the fight
> And what its issues mean."

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## THE PERCENTAGE OF STEMS IN BELLADONNA HERB AND ITS EFFECT ON THE QUALITY OF THE HERB.

By Arthur F. Sievers.

The Ninth Decennial Revision of the United States Pharmacopœia describes Belladonna Folia as follows: "The dried leaves and tops of *Atropa Belladonna* Linné (Fam. Solanaceæ), without the presence or admixture of more than 10 per cent. of its stems or other foreign matter, and yielding not less than 0.3 per cent. of the total alkaloids of Belladonna Leaves."

Previous to the ninth revision the stems were not allowed to be present. The change was brought about for two reasons. First, investigations had shown that belladonna stems not exceeding a reasonable size contain a considerable percentage of alkaloids; and second, the expense of harvesting the crop in this country is greatly

reduced by eliminating the expensive hand labor involved in picking the individual leaves. The change has aided greatly in stimulating the production of belladonna in the United States.

In connection with this change the question naturally arises as to what sized stems may be included when the herb is cut in order to limit the stems to 10 per cent. of the total herb. The inclusion of the stems makes harvesting by means of a sickle or large machinery possible, but by allowing only 10 per cent. of stems it becomes necessary in most cases to strip the material by hand in order to eliminate the larger stems. If it should be found that the inclusion of a greater percentage of stems does not greatly lower the therapeutic quality of the herb it would seem to be greatly to the interest of the grower to modify the official designation of the herb to that extent. It was for the purpose of securing some data on these questions that the following experiments were undertaken.

*Belladonna Herb at Various Stages of Growth.*—Sprouts of belladonna were cut at eight different stages of growth. The sprouts were cut at the ground and selected from different parts of the field to eliminate as far as possible the factor of individual variation. The sprouts were immediately weighed, a number of them were reserved to be studied as whole herb and the remainder were separated into leaves and stems both of which were weighed at once. All the parts were then allowed to dry in a well-ventilated room and finally in a hot air oven at 50° C. They were then weighed and ground to a no. 40 powder. A small quantity of the powder was dried over sulphuric acid to constant weight and the amount of residual moisture determined. All the results in the tables are calculated on the water free basis. In Table I are given the data relating to the proportion of stems in the herb.

It will be seen from the table that the eight stages represent a wide range of growth. At the first stage the sprouts were very small and the stems, while relatively large in diameter, were very short. On the other hand, at the last stage the stems were woody and the leaves were fewer in proportion. The moisture content of the stems does not appear to differ greatly in the first seven stages but in the last stage the pith was considerably less succulent which fact is indicated in the reduced moisture content. In the leaves, too, the moisture content is considerably lower in the last stage when the larger leaves are beginning to dry up somewhat. Likewise in the whole herb the percentage of moisture is considerably reduced in the last stage.

## TABLE I.

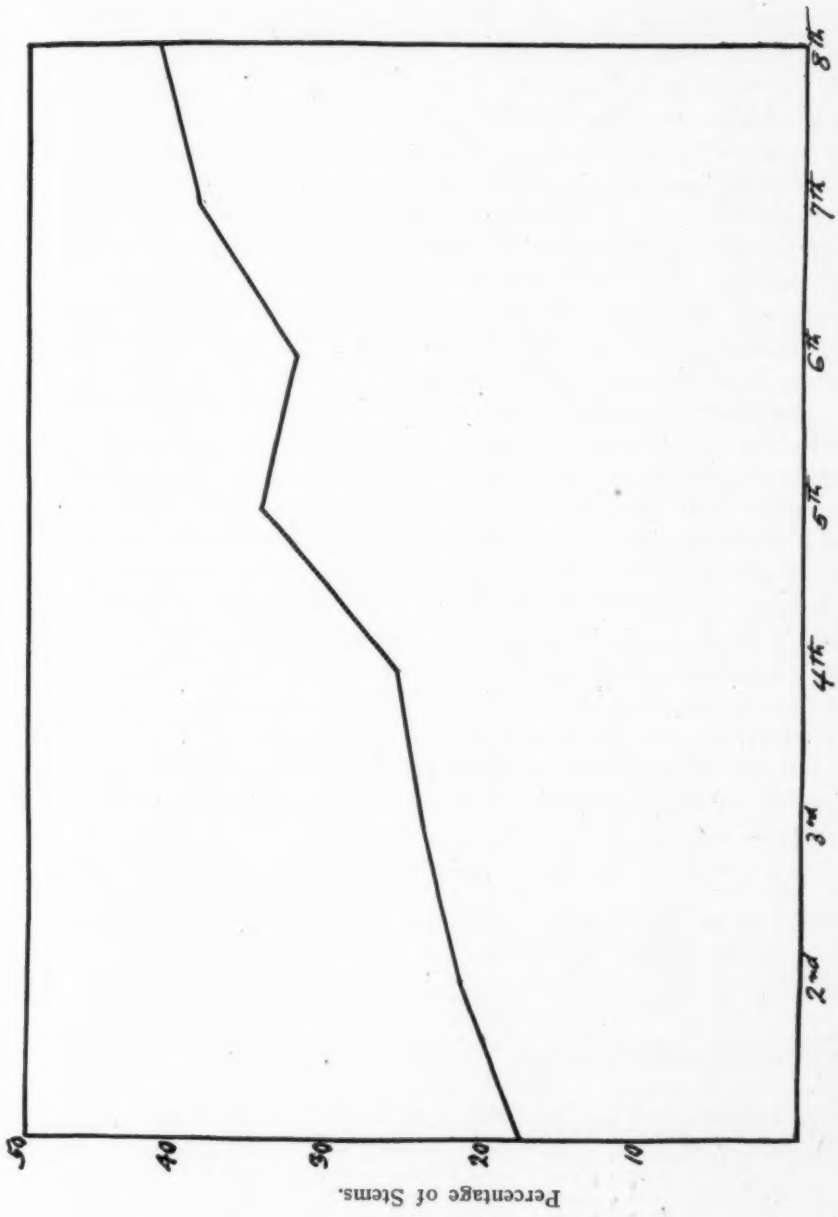
### Size and Proportion of Stems and Leaves in Sprouts Cut at Various Stages.

| Stage. | Sprouts. | | Stem. | | | | | Leaves. | | | Ratio of Dry Stems and Leaves in Sprouts. | | Whole Herb. | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Weight. | | | Weight. | | | | | Weight. | | |
| | No. Picked. | Length (Cm.). | Length (Cm.). | Diameter at Large End (Mm.). | Green (Gm.). | Dry (Gm.). | Moisture, Per Cent. | Green (Gm.). | Dry (Gm.). | Moisture, Per Cent. | Leaves, Per Cent. | Stems, Per Cent. | Green (Gm.). | Dry (Gm.). | Moisture, Per Cent. |
| 1 | 52 | 16.5–20 | 9–14 | 6–9.5 | 201.5 | 14.36 | 92.9 | 509.4 | 65.3 | 87.2 | 81.97 | 13.03 | 107.3 | 12.43 | 88.37 |
| 2 | 32 | 25 –29 | 15–20 | 8–10 | 253.5 | 16.58 | 93.46 | 449.8 | 59.72 | 86.72 | 78.27 | 21.73 | 154.3 | 15.38 | 90.03 |
| 3 | 28 | 29 –34 | 21–26 | 10–14 | 462.0 | 29.54 | 93.60 | 686.3 | 92.2 | 86.57 | 75.72 | 24.28 | 269.25 | 25.63 | 90.89 |
| 4 | 15 | 38 –43 | 31–34 | 14–16 | 503.3 | 28.06 | 94.43 | 660.5 | 80.54 | 87.81 | 74.16 | 25.84 | 310.55 | 30.34 | 90.23 |
| 5 | 10 | 55 –60 | 38–45 | 14–17 | 498.5 | 36.54 | 92.67 | 512.0 | 68.2 | 86.68 | 65.12 | 34.89 | 233.0 | 24.88 | 89.32 |
| 6[1] | 5 | 65 –70 | 50–55 | 16–18 | 450.9 | 29.69 | 94.07 | 372.5 | 60.94 | 83.64 | 67.24 | 32.76 | 413.0 | 38.03 | 91.79 |
| 7[2] | 6 | 80 –85 | 55–58 | 18–19 | 664.0 | 57.66 | 91.32 | 638.0 | 90.79 | 85.77 | 61.16 | 38.84 | 203.0 | 20.75 | 89.78 |
| 8[3] | 2 | 88 –100 | 50–58 | 18–19 | 334.0 | 56.49 | 83.09 | 435.0 | 79.37 | 81.75 | 58.42 | 41.58 | 534.0 | 86.6 | 83.78 |

[1] Fork with 3 sprouts 2 inches long at end of main stem.

[2] Fork with 3 sprouts about 3 to 6 inches long at end of main stem and at end of each of these a secondary fork with 2 or 3 sprouts 1 to 2 inches in length. A few flowers and many small buds present.

[3] Main fork of 3 or 4 sprouts about 6 inches long at end of main stem and a secondary fork at end of each of these with several sprouts 10 to 12 inches long. Flowers and green fruit and unopened inflorescence included in "leaves." Secondary sprouts were present at the axles of the large leaves. These had stems up to 10 inches in length and were separated into stems and leaves and mixed respectively with these parts from the main sprouts.




GRAPH I.—Percentage of Stems present in the herb at various stages.

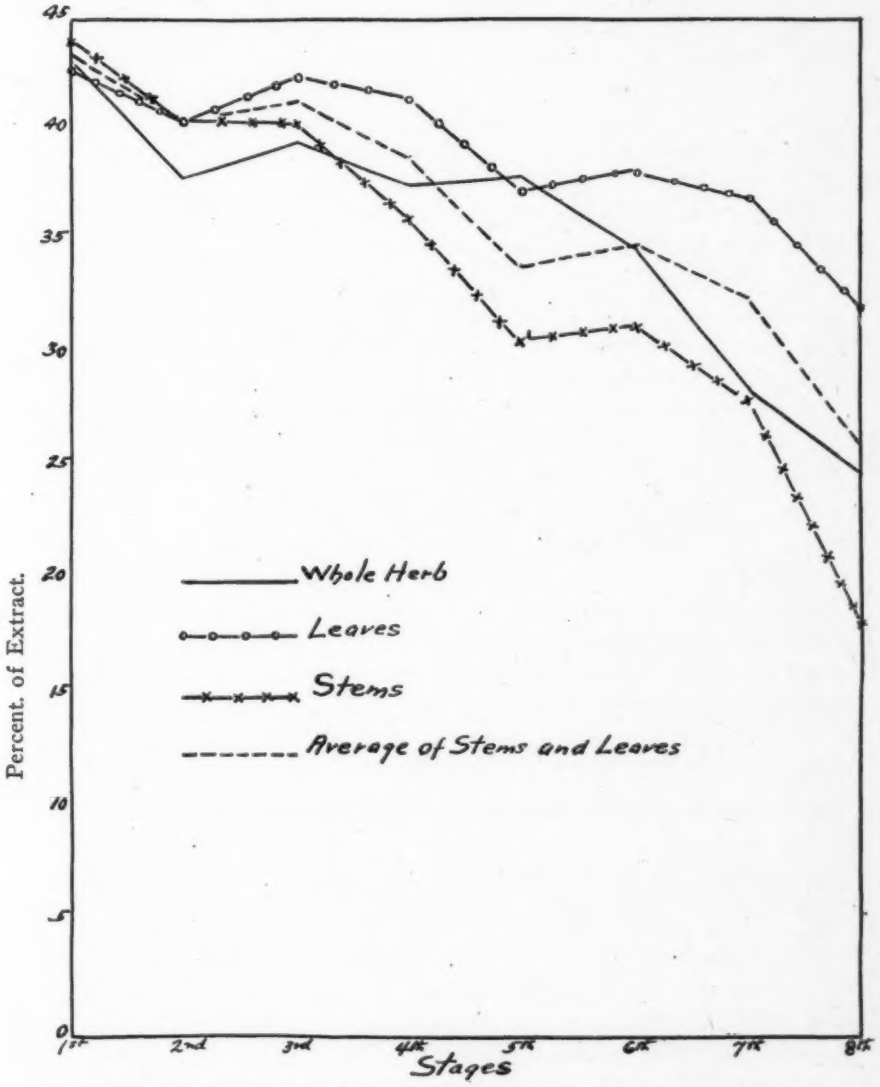
"A study of the table or of Graph I will show that in the smallest sprouts cut, the 1st stage, the stems represented 18 per cent. of the total dry weight. As growth continued this percentage gradually increased until it reached 41.58 per cent. at the eighth stage. Thus it will be seen that although the first material was picked when the stems were only 9 to 14 cm. long the percentage which these represent of the total dry weight is 8 per cent. more than allowed by the Pharmacopœia. It is evident, therefore, that in order to comply with the official description of belladonna herb machine harvested material cannot be used as such and must be resorted or stripped. It would seem therefore that the change made in the last revision of the Pharmacopœia has not been as great an aid in the matter of harvesting belladonna as might be desired.

The question naturally arises whether it would be possible to increase the permissible percentage of stems in the herb without greatly decreasing the therapeutic value of the herb. In order to determine this point the above samples of leaves and stems and whole herb were in each case assayed for total alkaloids and the percentage of alcoholic extract was determined. Ash determinations were also made to determine whether the ash content of the herb could be used as a basis for judging the percentage of stems present. The percentage of alcoholic extract was determined by means of the process described under "Extractum Belladonnæ Foliorum" of the Pharmacopœia. The extract was heated on a water bath until of constant weight and the percentage thus determined. No assay of these extracts were made. The results are given in Table II and Graphs II and III.

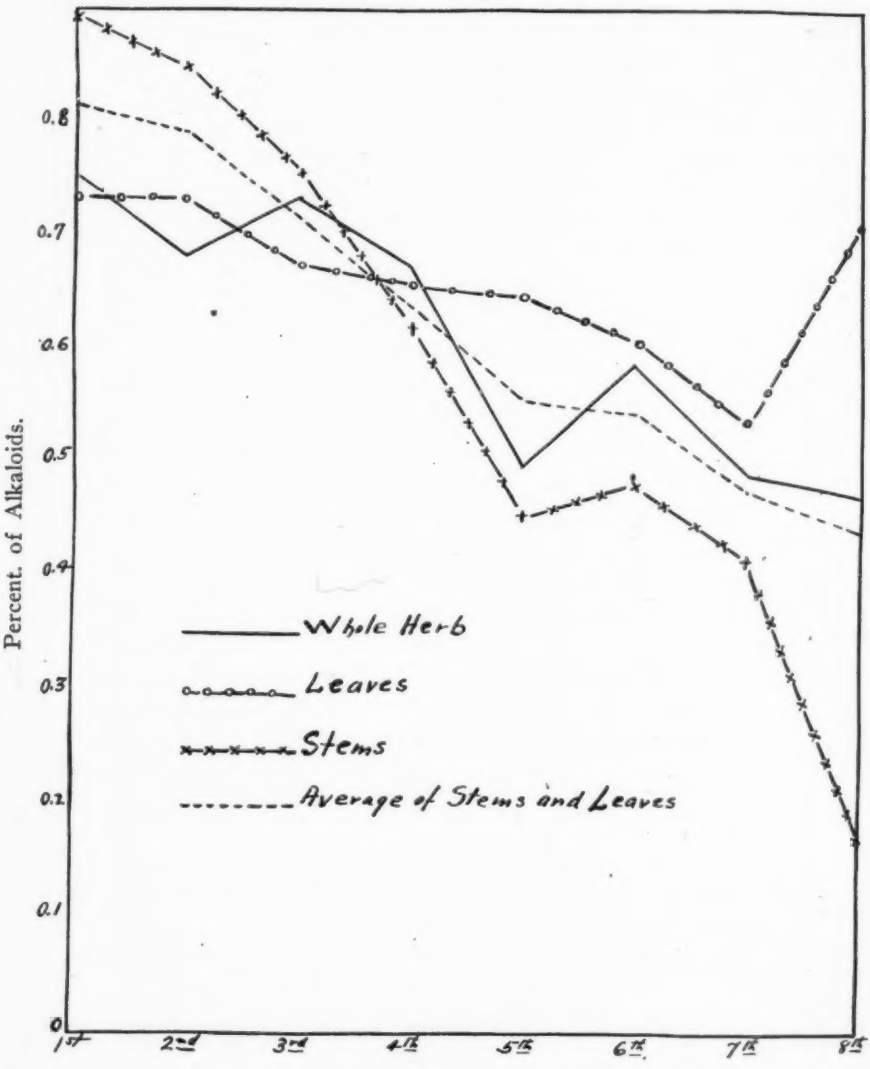
TABLE II.

PERCENTAGE OF ASH, ALCOHOLIC EXTRACTS, AND TOTAL ALKALOIDS IN THE STEMS, LEAVES, AND WHOLE HERB AT THE DIFFERENT STAGES.

| Stage. | Ash. | | | Alcoholic Extract. | | | Total Alkaloids. | | |
|---|---|---|---|---|---|---|---|---|---|
| | Leaves, Per Cent. | Stem, Per Cent. | Whole Herb, Per Cent. | Leaves, Per Cent. | Stem, Per Cent. | Whole Herb, Per Cent. | Leaves, Per Cent. | Stem, Per Cent. | Whole Herb, Per Cent. |
| 1 | 12.36 | 16.68 | 12.17 | 42.7 | 44.0 | 43.0 | 0.737 | 0.898 | 0.756 |
| 2 | 11.74 | 18.11 | 14.24 | 40.4 | 40.3 | 38.1 | .733 | .851 | .759 |
| 3 | 12.16 | 17.52 | 14.29 | 42.4 | 40.4 | 39.5 | .677 | .759 | .733 |
| 4 | 12.77 | 18.79 | 14.63 | 41.4 | 36.1 | 37.7 | .658 | .620 | .673 |
| 5 | 11.59 | 13.88 | 12.82 | 37.3 | 30.6 | 38.1 | .650 | .455 | .498 |
| 6 | 13.79 | 18.10 | 14.61 | 38.1 | 31.4 | 34.9 | .610 | .481 | .589 |
| 7 | 12.61 | 13.63 | 13.11 | 37.1 | 28.0 | 28.6 | .537 | .417 | .494 |
| 8 | 12.02 | 9.78 | 8.32 | 32.1 | 18.1 | 24.9 | .712 | .170 | .471 |




GRAPH II.—Percentages of Alcoholic Extract in the whole herb leaves and stems.




GRAPH. III.—Percentages of total Alkaloids in the whole herb, leaves and stems.

Regarding the ash content, there appear to be a number of inconsistencies in the results. The leaves show approximately the same ash content at all the stages but the stems seem to decrease in ash as they get larger. This is also true of the whole herb. It would seem doubtful from these results whether the ash content alone is a reliable criterion of the percentage of stems in the herb.

The percentage of alcoholic extract which can be obtained from the material decreases steadily from the first to the eigth stage. The stems show the greatest range in the amount of extract yielded, the highest being 44 per cent. at the first stage and the lowest 18.1 per cent. at the eighth stage. The leaves show a decrease of only about 10 per cent. from the first to the eighth stage. While the decrease in percentage of alcoholic extract is general it is evident from the tables and graphs that 25 per cent. of stems may be included in the herb without reducing the percentage of extract more than 6 per cent.

The percentage of total alkaloids also decrease through the different stages. This is decidedly marked in the stems, 0.898 per cent. being present at the first stage and 0.170 per cent. at the last stage. In the leaves the percentage decreases gradually and reaches the minimum of 0.537 per cent. at the seventh stage. At the eighth or last stage the percentage had increased again to 0.712 due, no doubt, to the presence of a considerable number of young leaves and shoots at this stage. The whole herb decreased in total alkaloids from 0.756 to 0.471 per cent., and at no stage was the percentage as low as the minimum set by the Pharmacopœia. The results plainly show that all the stems in the herb could be included in the sample without reducing the alkaloidal content below the pharmacopœial standard.

## Effect of the Presence of Various Percentages of Stems on the Quality of the Herb.

In the second part of this investigation an attempt was made to determine how the quality of the leaf is affected by the successive admixture of stems of certain diameter. A quantity of herb was cut at a stage corresponding to the eighth stage in the experiment previously described. The leaves, including all buds, flowers, and fruit, were immediately separated and weighed and designated as mixture A. The stems were then cut up into portions according to diameter and weighed and labeled successively from 1 to 8. Portion 1 consisted of stems from 2 to 3 Mm. in diameter while portion 8

consisted of the parts of the large stems from 17 to 20 Mm. in diameter. All portions were dried in a well ventilated room and finally in a hot-water oven. The last traces of moisture were determined by drying the powdered material over sulphuric acid to constant weight. Table III gives a summary of the various portions of stems.

TABLE III.

MOISTURE CONTENT AND DIAMETER OF THE STEMS IN THE EIGHT SUCCESSIVE PORTIONS.

| Portion. | Diameter (Mm.). | Weight. | | Moisture, Per Cent. |
|---|---|---|---|---|
| | | Green (Gm.). | Dry (Gm.). | |
| 1 | 2–3 | 96.7 | 17.56 | 82.25 |
| 2 | 3–5 | 100.0 | 18.53 | 81.47 |
| 3 | 5–6 | 91.0 | 17.00 | 81.32 |
| 4 | 6–9 | 142.0 | 25.38 | 82.13 |
| 5 | 9–12 | 119.0 | 20.61 | 82.77 |
| 6 | 12–14 | 136.0 | 28.30 | 79.19 |
| 7 | 14–17 | 151.0 | 21.80 | 85.57 |
| 8 | 17–20 | 186.0 | 31.94 | 82.83 |

After the portions were all thoroughly dry they were ground as finely as possible and then added successively to mixture A. After the addition of each portion the percentage of ash, alcoholic extract, and alkaloids were determined. In Table IV the results are summarized.

It is obvious from Table III that the stems in portion 8 weigh almost twice as much as those from portion 1. In a general way there is a gradual increase in the weight of the dry stems in the successive portions. The percentage of moisture is approximately the same in all the portions.

As indicated in Table IV the percentage of ash, alcoholic extract and total alkaloids of mixture A were first determined. This mixture included only the very small stems up to 2 Mm. in diameter which forms a part of the flowering top. To A was then added portion 1 which consisted of stems from 2 to 3 Mm. in diameter. After thorough mixing the percentage of ash, alcoholic extract and total alkaloids were again determined. To this mixture portion 2 was then added and so on until all the portions had been successively added. The final mixture then approximately represented the whole herb. Graph IV shows the percentage of stems present in the mixture after the addition of each successive portion.

It will be noted that if a maximum of 10 per cent. of stems is

TABLE IV.

PERCENTAGE OF ASH, ALCOHOLIC EXTRACT AND TOTAL ALKALOIDS IN SUCCESSIVE MIXTURES OF MIXTURE A WITH PORTIONS 1 TO 8 OF THE STEMS.

| Mixture. | | Per Cent. of Total Stems Present. | Ash, Per Cent. | Alcoholic Extract, Per Cent. | Alkaloids, Per Cent. |
|---|---|---|---|---|---|
| No. | Nature. | | | | |
| A | Leaves[1] | — | 13.84 | 26 | 0.580 |
| B | A + portion 1[2] | 6.51 | 10.2 | 26 | .586[3] |
| C | B + portion 2 | 12.53 | 10.11 | 27.6 | .572 |
| D | C + portion 3 | 17.07 | 10.05 | 25.8 | .519 |
| E | D + portion 4 | 23.74 | 9.46 | 22 | .510 |
| F | E + portion 5 | 28.22 | 9.28 | 21.4 | .478 |
| G | F + portion 6 | 33.57 | 9.09 | 21.8 | .456 |
| H | G + portion 7 | 37.01 | 8.83 | 20.00 | .345 |
| I | H + portion 8 | 41.82 | 8.71 | 21.2 | .336 |

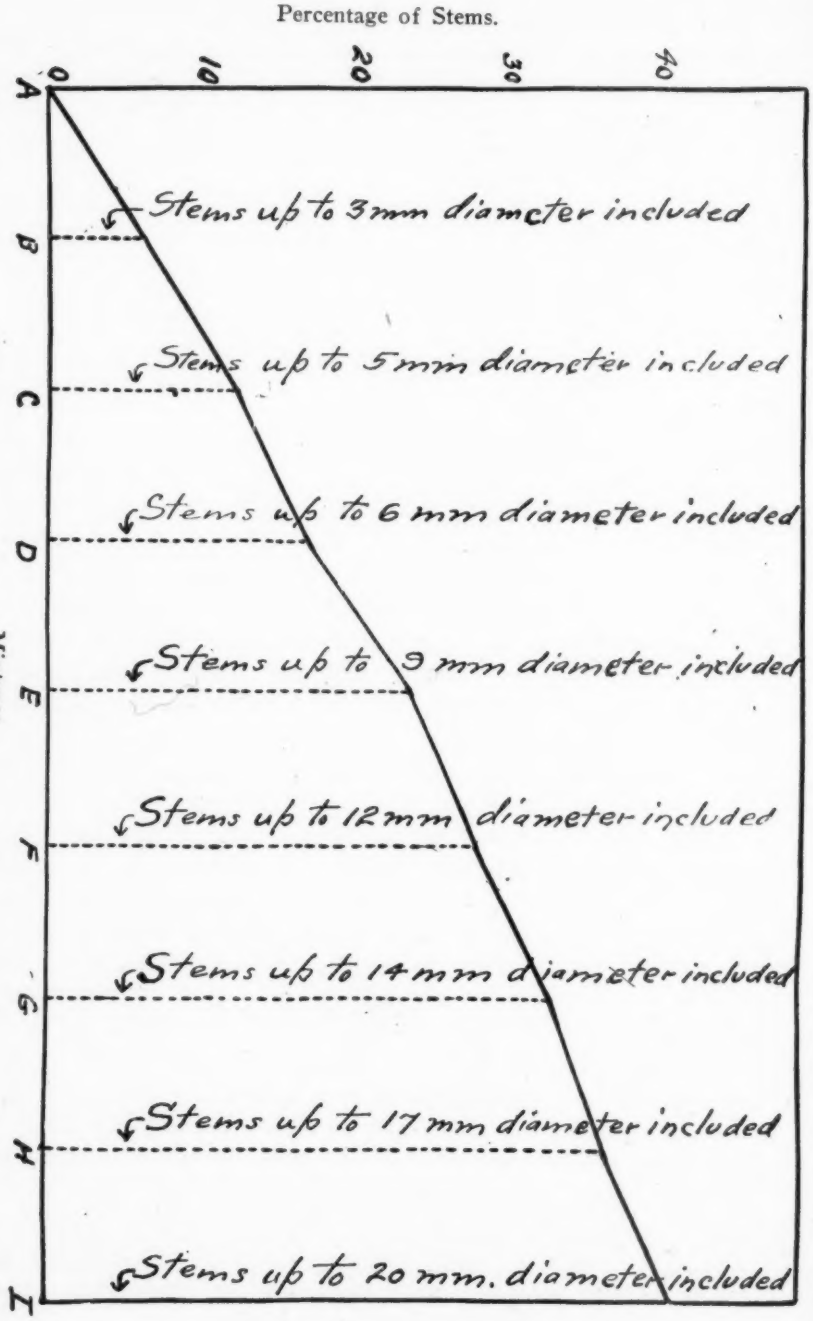
allowed in the herb all stems above 5 Mm. in diameter will have to be excluded. The percentage of ash decreases with the admixture of more stems from 13.84 to 8.71 per cent. The percentage of alcoholic extract also decreases slowly from 26 to 21.2 per cent. while the percentage of total alkaloids decreases from 0.58 to 0.336 per cent. Graphs V and VI serve to illustrate these points. Here again it is shown, as in the first part of the paper, that all the stems could be included in the herb and the percentage of alkaloids would still be higher than the minimum allowed in the Pharmacopœia. However, where a poor quality of herb is involved in which the percentage of total alkaloids is low the addition of all the stems would very likely reduce the percentage too far.

Taking a fair quality of herb such as is readily produced in this country, as an example, a mixture of approximately the composition of D or E should be a very marketable product. Such an herb would contain about 20 per cent. of stems up to 7 or 8 Mm. in diameter when green. It would contain about 10 per cent. of ash,

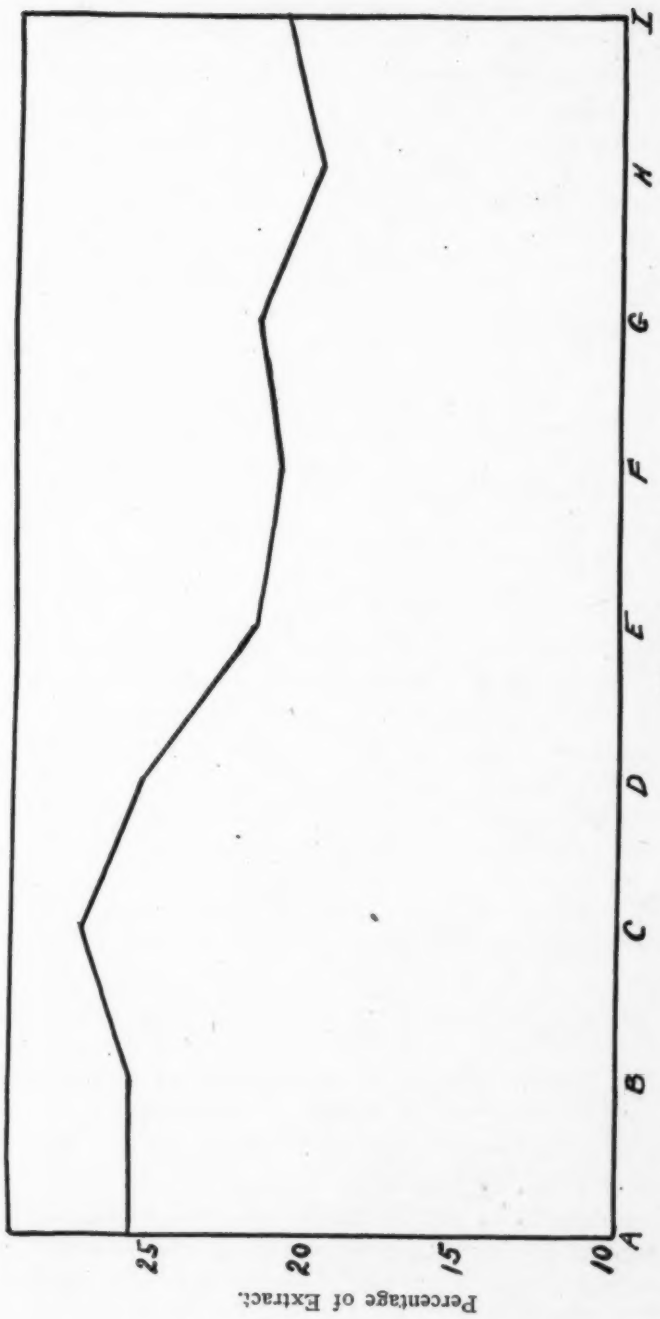
[1] Consists of all leaves and buds, flowers, and berries but contains no stems more than 2 mm. in diameter.

[2] See Table III.

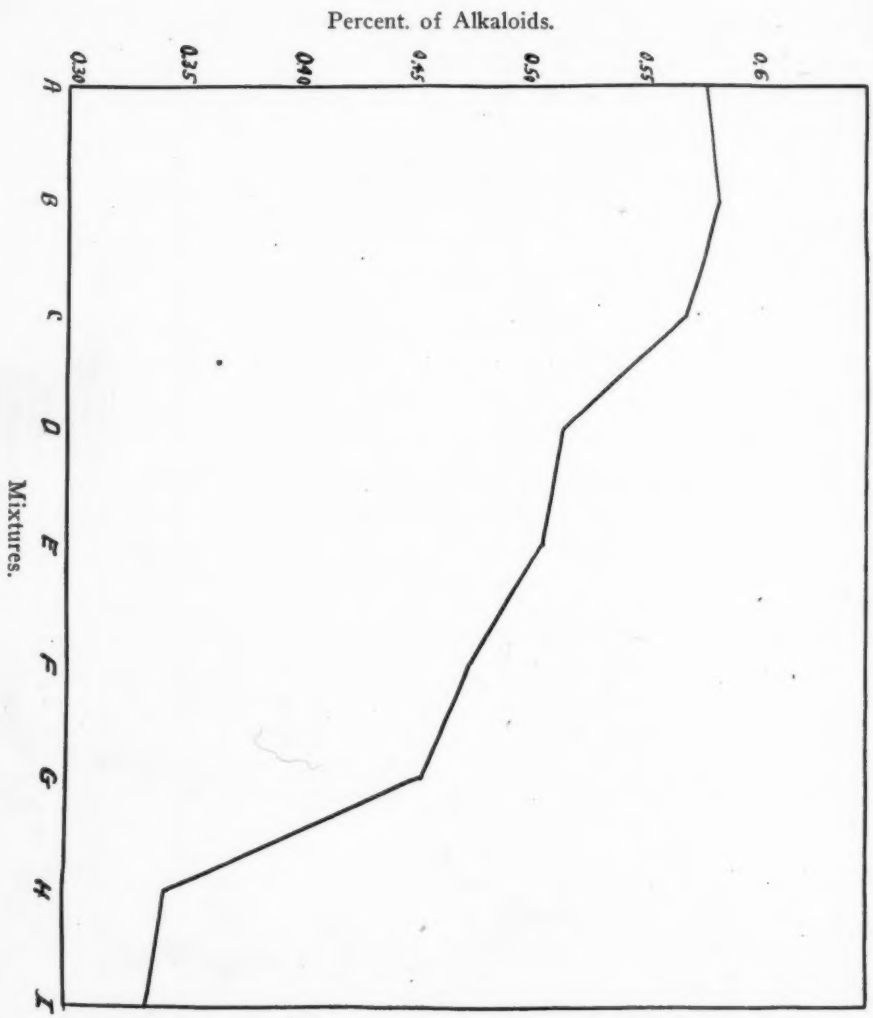
[3] Since approximately 10 to 12 Gm. of material had to be removed after the addition of each portion to make the several determinations, the influence of the addition of the succeeding portion of stems is slightly intensified, and consequently, since the effect of adding the stems is to reduce the percentage of alkaloids, the percentage as found is slightly lower than it would have been if no small fraction of the previous mixture has been removed. However, inasmuch as the percentages actually obtained are thereby reduced the conclusions based on these results are in no wise affected. This is equally true in the case of the alcoholic extract and the ash.




GRAPH IV.—Percentage of Stems in successive mixtures and the maximum diameter of the stems included in each.




GRAPH V.—Percentages of Alcoholic Extract in the successive mixtures.




GRAPH VI.—Percentages of total Alkaloids in the successive mixtures.

about 23 per cent. of alcoholic extract, and about 0.5 per cent. of total alkaloids.

There seems no good reason why such a product should not be entirely suitable for practically all purposes for which belladonna is marketed. If such is the case there would appear to be full justification for increasing the percentage of stems allowed to 20 per cent. provided it is not made possible thereby to increase the

foreign matter to a similar extent. Instead of stating that the herb should be "without the presence or admixture of more than 10 per cent. of its stems or other foreign matter," it would seem advisable to permit a maximum of 5 per cent. of foreign matter and to allow the presence of 20 per cent. of belladonna stems as a maximum.

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# THE DETERMINATION OF MORPHINE IN COMPLEX PRODUCTS.

## Part III. Opium and Mixtures Containing Opium.

By Alfred Tingle, Ph.D.

### Introduction.

The very large number of methods which have been proposed for the determination of morphine in opium is in itself a strong argument that a reliable one is yet to be sought. Moreover, not one of these is capable of simple extension to cover combinations other than opium itself. Even when used on such closely allied derivative as a tincture or fluid extract, a new set of arbitrary corrections must be empirically determined and introduced into the calculation of the results.

To apply such methods to mixtures of unknown composition would be out of the question on that account alone. Further, they cannot be applied to pills containing some of the excipients mentioned in Part II of this communication, as the resulting mixtures would be colloidal suspensions which could neither be filtered nor even dealt with by decantation.

Many of the methods proposed, and even in common use, are necessarily inaccurate, in view of our more recent knowledge of opium. For instance, L. Debourdeaux (*Bull. Sci. Pharmacol.*, 1910, XVII, 382–385) has shown that as much as 10 per cent. of the morphine in opium is in a form insoluble in water and alcohol, and only to be rendered soluble by an alkali or alkaline earth. Thus the method laid down in the United States Pharmacopœia is quite vain.

Of those methods which direct that morphine be extracted by lime, that of Douzard (*Pharm. J.*, 1903 [IV], 17, 909–910) is a popular one. It suffers from a fundamental error in reckoning that 1 Cc. of $\frac{N}{10}H_2SO_4 = 0.0283$ gramme of anhydrous morphine. Reference to experiments 1 and 2 in Part I of this communication will show that the figure derived directly from theory is correct.

An objection against all methods in which lime is used is that while aliquot parts of the extract are taken for the determination, these are reckoned on a basis other than that of their relation to the water known to be present: instead of the mixture of opium, lime, and water being made to a measured volume, it is a measured volume of water which is added. An irregularity in the amount of water previously present, or formed in the reaction, will thus produce a corresponding error.

In all these methods, the morphine is precipitated in the presence of alcohol, and sometimes the proportion of alcohol is large. The magnitude of the errors to which this gives rise is fairly well known, and is again displayed in Experiments 8, 9 and 10, Part I of this communication. Many standard methods introduce fixed corrections to meet this loss. Douzard (*loc. cit.*) adds 0.05 Gm. of anhydrous morphine to the amount found by titration in a reputed 4 Gm. of opium, *i. e.*, 1.25 per cent. Stevens (*Pharm. Arch.*, V, 41–45) adds 1.12 per cent. to the percentage of crystallized morphine found by his titration. The British Pharmacopœia does not specify a correction, but admits a possible error of — 1 per cent.

In the latter case, even if the solvent effect of alcohol and ether be disregarded, the loss through water alone (of which 104 Cc. is present) cannot be less than 0.65 per cent. as shown in Part 1, Experiment 12.

"Corrections" of this order of magnitude, which represent about 10 per cent. of the morphine present in average opium, must give rise to grave doubts of the accuracy obtained. Furthermore, it makes it impossible to use such methods when the percentage of morphine is small, and analyses of opium are on record showing as little as 2 per cent. of morphine. The writer himself has examined a sample of smoking opium which gave no morphine when submitted to the United States Pharmacopœia method of estimation, so small was the actual proportion and so great the errors of the procedure. Yet this sample was obtained from an illicit dealer whose

product was reputed to be stronger and purer than that of the shops licensed by the Chinese government.

It is not easy to see why such a state of affairs with respect to the assay of opium and the determination of morphine in opium products has been allowed to continue. That existing methods are intended for trade purposes only is not an answer, since it is for trade purposes that some of our most accurate analytical methods in other fields have been designed. Morphine has so high a value commercially that its accurate determination must be financially important. Yet it seems as though a lower standard than should be allowed has hitherto been set. Betterment is demanded both in the interests of business enterprise and by scientific pride.

In the present work the writer has been urged by necessities rising from successive official positions which he has held. The results here presented do not constitute a complete solution of the problem, but they appear to approach nearer to that end than any yet brought forward.

## Principles of the Proposed Method.

The manner of determining morphine described in Part II of this communication cannot be applied to opium and its preparations, since the extraction by a chloroform-alcohol mixture would separate resinous matter, some of which has a basic character, with the morphine. This resinous matter also accompanies the morphine when the latter is precipitated from alkaline solution by the addition of an ammonium salt, unless alcohol be present, in which case a serious loss of morphine occurs. But a great part of this resin is precipitated on cooling after the aqueous solution containing it has been digested with salicylic acid. This procedure does not affect the morphine, but is not in itself a complete purification. The alkaloid must be precipitated from a concentrated solution in the presence of chloroform, no alcohol being used; it is then further purified by re-solution and extraction with a chloroform-alcohol mixture.

The only necessary cause of loss in the whole process is the precipitation, and the extent of such loss is much less than in other methods. The chemical justifiability of each step can be seen by reference to the data collected in Part I of this communication.

The method now to be set forth can be applied equally well to

dry or moist opium, to opium ash (so often a constituent of Chinese pills for the "cure" of the opium habit) or to complex pills containing these substances. The exceptions to this statement arise from the presence of "interfering" compounds, usually inorganic, and with ordinary ingenuity such exceptions can be met by slight elaborations of the procedure. Such a case is that of "Dover's Powder," the examination of which is detailed under Experiment 38.

Since calculation of the results involves no consideration but that of the obvious stoichiometrical relations, no special factors are used.

### Detailed Description of the Method.

A convenient weight for the sample is 6 Gm. This is placed in a flask graduated to contain 100 Cc. and is digested for 10 minutes on the water bath with 2 Gm. (approximately) of calcium carbonate and enough water to form a thin paste. While warm, the flask should be lightly closed with a rubber stopper. After digestion, the flask is cooled, and 60 Cc. of a cold saturated solution of barium hydroxide is added. The flask, now closely stoppered, is well shaken at intervals. After 20 to 30 minutes water is added to bring the total volume to 100 Cc. The solution is filtered through a dry 15 Cm. paper, and an aliquot portion of the filtrate (50 Cc.) is transferred to a flask graduated to contain 55 Cc. [meantime the residue on the filter may be examined for meconates as described in Part II].

Sulphuric acid (diluted 1:5) is added by drops till the solution is faintly acid and no more precipitate forms, the flask being warmed on the water bath to promote settlement. The solution is next made faintly alkaline by the cautious addition of concentrated sodium hydroxide solution. Salicylic acid is next added, in crystals, till acidity is restored, the flask being warmed after each addition to induce rapid solution of the acid. When an acid reaction has developed, the further quantity of 0.5 Gm. of salicylic acid is added and the flask is heated for 10 minutes by immersion in boiling water. It is allowed to cool to normal temperaure, and enough water is added to bring the contents to 55 Cc. The liquid is filtered through a dry 7 Cm. paper, and an aliquot portion of the filtrate (preferably 50 Cc.) is taken for further operations.

The clear solution is evaporated on the water bath (best in a

platinum dish) almost to dryness. The dish is cooled and enough water is added to make the volume of its contents as nearly as possible 5 Cc. To this is added 5 Cc. of chloroform and about 3 drops of concentrated ammonium hydroxide solution or as much more as is needed to produce decided alkalinity. The liquids are well mixed with a stirring rod which is caused to scratch the bottom of the dish lightly and to break up undissolved aggregates, thus promoting rapid precipitation of the morphine. When the latter substance begins to separate the dish is covered and set aside for four hours, during which time it should be occasionally agitated with a rotary motion.

The contents of the dish are filtered through a cotton plug with the aid of suction, the dish and morphine being washed with small quantities of cold water (morphinated water may be substituted at the analyst's discretion) till the washings become colorless. About 10 Cc. of water, if care is used, should suffice for this washing, in most cases.

The morphine thus obtained is yellowish and not pure enough to give reliable results on titration. The plug with adherent alkaloid is lifted into a small separating funnel. The morphine remaining in the dish is dissolved in a small quantity of dilute sulphuric acid and the solution is transferred to the separating funnel through the funnel previously used for the filtration. The dish and funnel are then well washed with water. Washings and acid together should not exceed 20 Cc.

The solution of morphine is made sufficiently alkaline to liberate all the alkaloid by the addition of either a few drops of concentrated ammonium hydroxide or a saturated solution of sodium hydrogen carbonate. It is then shaken for 3 minutes with 25–30 Cc. of chloroform-alcohol mixture (2 volumes of chloroform to 1 volume of alcohol). After separating the lower layer of liquid, the extraction is exactly repeated on the aqueous layer with three further similar quantities of the chloroform-alcohol mixture, the time of shaking being 3 minutes in every case.

The combined extracts are distilled on the water bath. The residue of almost white morphine is dissolved in a known volume of decinormal sulphuric acid, the excess of which is titrated with decinormal or twentieth-normal sodium hydroxide. Lacmoid, cochineal or methyl orange are suitable indicators.

The weight of morphine found by this titration will be 10/22 of

that present in the original 6 Gm. sample, if the aliquot parts taken were those recommended above.

### Remarks.

The weight of sample and the particular relative magnitude of the aliquot parts chosen may be varied accordingly to the circumstances of the case, but the above-mentioned quantities have proved generally convenient. It is important to note, however, that at the outset more than half the total volume of liquid used should consist of cold saturated barium hydroxide solution, and the morphine should be precipitated, in the later stage, from the most concentrated solution possible.

Even under the most favorable conditions some morphine will remain in solution, after precipitation of the main quantity. If it is desired, a correction (+ 0.26 Cc. $\frac{N}{10}$ acid) derived from experiment 11 (Part I) may be made to the titration result. In such case it is necessary to adhere strictly to the conditions of precipitation and washing here laid down. There are decided objections to making such corrections, and probably they are best omitted. The relative importance of this error may be reduced by increasing the weight of sample worked with.

### Comparison with Other Methods.

Since the results given by most standard methods must be considered uncertain to at least the extent of 0.5 per cent., serious comparisons are somewhat lacking in interest.

The opium used in Experiments 31, 32 and 33 was, however, examined by the method of Stevens (*Pharm. Arch.*, V, 41–45) modified by doubling the quantities specified by him. The result thus found was 10.42 per cent., which is materially less than that given by the experiments quoted.

It must be remembered that extraction by barium hydroxide is likely to be more thorough than by lime, while the analytical losses in the new method are notably less.

### Experimental Data.

*Examination of Opium. Experiment 31*[1].—The material used purported to be a Persian opium. A sample of 6.0000 Gm. was

[1] These experiments are numbered consecutively with those in Parts I and II.

treated according to the method described above, the volumes of liquid employed being those there mentioned. The morphine found by titration was therefore 10/22 of the whole, or that present in 30/11 Gm. of opium.

TITRATION RESULTS.

| | |
|---|---|
| Total acid used | = 26.00 Cc. |
| Acid equivalent to the alkali | = 15.65 Cc. |
| Acid equivalent to the morphine | = 10.35 Cc. |
| Since 1 Cc. acid = 0.0300 Gm. $C_{17}H_{19}NO_3 \cdot H_2O$ crystallized morphine found | = 0.3105 Gm. |
| | = 11.3 Per Cent. |

*Experiment 32.*—This was a check determination, duplicating Experiment 31.

TITRATION RESULTS.

| | |
|---|---|
| Total acid used | = 25.00 Cc. |
| Acid equivalent to the alkali | = 14.71 Cc. |
| Acid equivalent to the morphine | = 10.29 Cc. |
| Crystallized morphine found | = 0.3087 Gm. |
| | = 11.32 Per Cent. |

*Experiment 33.*—The material used was the same, but the method of operation differed in two details. (1) Salicylic acid was used in larger quantity (2 Gm. excess instead of 0.5 Gm. previously taken), and (2) the volume taken of the filtrate from the barium sulphate was only 45 Cc. The morphine found by titration thus represented only 9/22 of the whole amount in the original sample.

TITRATION RESULTS.

| | | |
|---|---|---|
| Total acid used | | = 25.00 Cc. |
| Acid equivalent to the alkali | | = 15.58 Cc. |
| Acid equivalent to the morphine | | = 9.42 Cc. |
| Crystallized morphine found | | = 0.2826 Gm. |
| | or | = 11.51 Per Cent. |

*Experiment 34.*—This determination was made upon material believed to be of Indian origin. The method used and quantities taken were the same as in Experiments 31 and 32. The determination was made in duplicate.

TITRATION RESULTS.

| | I. | II. |
|---|---|---|
| Total acid used | = 25.00 Cc. | 25.00 Cc. |
| Acid equivalent to the alkali | = 14.71 Cc. | 14.51 Cc. |
| Acid equivalent to the morphine | = 10.29 Cc. | 10.49 Cc. |
| Corresponds to grammes of crystalline morphine | 0.3087 | 0.3147 |
| or crystalline morphine in whole | 11.32 Per Cent. | 11.54 Per Cent. |

*Examination of Smoking Opium. Experiment 35.*—The material under examination was smoking opium which had been allowed partly to dry in the air. In consequence of the superficial drying it was difficult to obtain two samples which were true duplicates. This difficulty was overcome by taking a single large sample, which was weighed into a tared beaker, dissolved in warm water and washed into a graduated (250 Cc.) flask. After cooling, 150 Cc. of cold saturated barium hydroxide solution was added, and the mixture made to the mark with cold water. It was allowed to stand 20 minutes and filtered. Two portions of 50 Cc. each were taken from the filtrate, and the analysis of each was continued independently by the method used in Experiment 31.

Total weight of opium taken = 16.4180 Gm. Weight corresponding to each 50 Cc. of alkaline solution = 3.2836 Gm.

TITRATION RESULTS.

| | I. | II. |
|---|---|---|
| Total acid used | = 25.00 Cc. | 25.00 Cc. |
| Acid equivalent to the alkali | = 13.75 Cc. | 13.85 Cc. |
| Acid equivalent to the morphine | = 11.25 Cc. | 11.15 Cc. |
| Corresponds to grammes of crystalline morphine | 0.3375 | 0.3345 |
| or crytalline morphine in whole | 11.30 Per Cent. | 11.20 Per Cent. |

A determination of water in the above opium was subsequently made.

| | |
|---|---|
| Weight of moist sample | 2.3116 Gm. |
| Weight of dried sample | 1.9196 Gm. |
| Weight of water found | 0.3920 Gm. |

The above corresponds to 16.95 per cent. water, which is considerably less than is found in opium freshly prepared for smoking.

From the above results the mean morphine content of the dry product would be 13.55 per cent.

*Examination of "Opium Ash" or "Opium Dross" (Ta Yen Hui).* *Experiment 36.*—The method of analysis applied to the foregoing samples was used in this case on a sample of opium ash. The details of the operation exactly resembled those of Experiment 31. It may be remarked that, though opium ash contains so much resinous matter, the morphine for titration appeared as pure as that obtained in the same way from opium itself.

TITRATION RESULTS.

| | |
|---|---|
| Total acid used | = 25.00 Cc. |
| Acid equivalent to the alkali | = 17.71 Cc. |
| Acid equivalent to the morphine | = 7.29 Cc. |

Corresponds to 0.2187 Gm. crystalline morphine or 8.02 Per Cent.

*Examination of Pills containing Opium, such as might be sold "For Curing the Opium Habit."* *Experiment 37.*—The sample was made up of 5.4 Gm. of Chinese pill mass and 0.6000 Gm. of the same opium as that used in Experiments 31, 32 and 33.

TITRATION RESULTS.

| | |
|---|---|
| Total acid used | = 10.00 Cc. |
| Acid equivalent to the alkali | = 9.25 Cc. |
| Acid equivalent to the morphine | = 0.75 Cc. |

Corresponds to 0.0225 Gm. of crystallised morphine or 0.82 Per Cent.

Calculated from the mean result of Experiments 1, 2 and 3 the result should have been 1.14 per cent. or 0.32 per cent. higher. The precipitate, produced at the beginning of the analysis by the addition of barium hydroxide, was washed into a casserole and acidified with an excess of hydrochloric acid. After boiling for a few minutes the product was filtered. This filtrate was concentrated to a convenient volume and tested with ferric chloride solution. It gave the color characteristic of meconic acid very distinctly.

*Examination of "Dover's Powder."* *Experiment 38.*—The same method of determining morphine was applied to "Dover's Powder" with such modification as becomes necessary when a large proportion of sulphates is present in the material under examination.

The Dover's Powder used only differed from the "B. P." preparation in that the opium was slightly above the official strength. The mixture was composed of 4.8000 Gm. of potassium sulphate, 0.6000 Gm. of powdered ipecacuanha root, and 0.6000 Gm. of the opium used in Experiment 31. Total weight of mixture 6 Gm.;

morphine 1.14 per cent. This was placed in a graduated (200 Cc.) flask and digested on the water bath with 20 Cc. of water for 10 minutes. An aqueous solution containing 9 Gm. of barium chloride was added, followed by 120 Cc. of a cold saturated barium hydroxide solution. After standing 30 minutes the mixture was diluted to 200 Cc. The remainder of the determination was carried out in the manner already described, but 100 Cc. was substituted for 50 Cc. and 110 Cc. for 55 Cc. when taking an aliquot part and later diluting.

TITRATION RESULTS.

| | |
|---|---|
| Total acid used | = 10.00 Cc. |
| Acid equivalent to the alkali | = 9.27 Cc. |
| Acid equivalent to the morphine | = 0.73 Cc. |

Corresponds to 0.0219 Gm. of crystalline morphine, or 0.80 Per Cent.

Calculated from Experiments 31, 32 and 33, the result should have been 1.14 per cent., *i. e.*, 0.34 per cent. higher.

Titration with acid of anything like decinormal strength is obviously not a suitable method for the accurate determination of such small amounts of morphine as were present in this case and in Experiment 37, but it serves sufficiently to show how far the present method of separating morphine can be applied.

If the correction mentioned on p. 856 be applied to Experiments 31, 32, 33, 37 and 38, we get figures in closer agreement, as follows.

| | | | | |
|---|---|---|---|---|
| Experiment | 31. | Morphine | 11.67 Per Cent. | } Mean 11.70 Per Cent. |
| " | 32. | " | 11.60 Per Cent. | |
| " | 33. | " | 11.83 Per Cent. | |
| " | 37. | " | 1.10 Per Cent. | } Calculated 1.17 Per Cent. |
| " | 38. | " | 1.09 Per Cent. | |

ACKNOWLEDGMENT.

In the course of this work, which was commenced in China in 1909, I have received direct and indirect help from friends and colleagues too numerous to mention, but notably from Mr. F. W. Babington, chief analyst in this laboratory, Mr. Allan A. Ferguson, at one time a member of its staff, and Hu Ch'ing T'ang.

Without the unfailing kindness, consideration, and helpfulness of the former, the work could not have been continued. Mr. Ferguson assisted with many experiments under my supervision: none of

them are recorded here, but they opened the way for later work. The services of Hu Ch'ing T'ang were invaluable in earlier days, especially in the collection of curious material, and to him I owe much of my knowledge of the intricate ways of opium dealers (legal and illicit) of China, and my appreciation of the problems these cause to be presented. To these and to others not named, I wish to render my grateful thanks.

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## HAZLITT ON THE METRIC SYSTEM.

BY JAMES F. COUCH.

English thinkers have, as a general rule, always been opposed to the adoption and use of the metric system in spite of its, to us, obvious advantages over the cumbrous and time-wasteful inch, pound, gallon measures in use by Anglo-Saxon countries. The obstinacy with which they reject efforts to substitute the metric for the English system must be due, in large part, to native prejudice and conservatism which rejects innovations that appear experimental and resists, through intellectual inertia, all fundamental changes in the established order of things. Unfortunately, from its very nature, the metric system must be adopted by any people in its entirety at one time: in a moment there must be a change from the old system to the new, a revolution which cannot help but cause confusion in practically all the industries. The metric system does not admit of a gradual adoption, replacing the English system little by little and so permitting the great mass of business men and traders to become accustomed to it in the slow method by which most great revolutions in human thought and activity are brought about.

Over a decade ago the views of Herbert Spencer,[1] that giant of British intellectuality, were published in this journal by Florence Yaple. In that paper Spencer presents what is probably the strongest case against the metric system ever written. I wish to quote here the argument against the metric system advanced by another British philosopher because it considers the case from an entirely different

[1] This JOURNAL, 76, 125–128.

aspect and one which is more likely to affect the people than the point of view taken by Spencer.

William Hazlitt was born at Maidstone, England, on the tenth of April, 1778, and died on the eighteenth of September, 1830. He was thus, as Spencer was not, a contemporary of the changes in France which brought about the introduction of the metric system. His reputation was founded on many literary, historical, and philosophical essays. His style is vigorous; his thought clear; his attitude strongly tinctured by prejudices. The following quotation is taken from his "Life of Napoleon Buonaparte," Chapter 15, page 375.

"Nothing renders a government unpopular or excites hatred and contempt sooner than a disposition to interfere in trifles, and without any reason but the itch of governing. The new system of weights and measures was another grievance complained of. The want of uniformity in French weights and measures was an inconvenience that had long been felt; and it was expected among other things that the revolution would have corrected this evil. The remedy was in fact simple and at hand; it was to render the system of weights and measures in use in the city of Paris, and which had also been employed by the government and artists for centuries, common throughout all the provinces. Instead of this, the government, who at that time did everything on a grand scale of abstraction, consulted the algebraists and geometricians upon a question of practical utility who soon hit upon a system which neither agreed with the regulations of the public administration, with the tables of dimensions used in all the arts, nor with those of any of the existing machines. Nor would other nations have agreed to this, which was meant to be a universal benefit to the world. What would the English, for instance, have said to it? The new system not only was at variance with common sense and custom, and required all the calculations of the arts and sciences to be reversed, but was in itself impracticable and unintelligible. It converted the commonest affairs of life into an abstruse mathematical calculation. Thus a soldier's ration is expressed by twenty-four ounces in the old nomenclature; this is a very simple process; but when translated into the new one, it becomes seven hundred and thirty-four grammes and two hundred and fifty-nine thousandths. All the dimensions and lines that compose architectural works, all the tools and measures used in clock making, jewellery, paper making, and the other mechanic arts, had been invented and calculated according to the ancient nomenclature,

and were expressed by simple numbers, which must now be represented by five or six figures. Another disadvantage was that the savants introduced Greek roots, which farther multiplied difficulties; for these denominations, though they might be useful to the learned, only perplexed the common people. But the Directory made the weights and measures one of the principal affairs of government. Instead of leaving it to time to work the change, and merely encouraging the new system by the power of example and fashion, they made compulsory laws and had them rigorously executed. Merchants and artisans found themselves harassed about matters in themselves indifferent; and this increased the unpopularity of a government which placed itself above the wants and the reach of the people, infringing on their habits and usages with all the violence which might be expected from a Tartar conqueror. It is always bad policy in a government to meddle more than it can help with the affairs of private life, which individuals understand so much better than mere theorists, thus subjecting itself at once to the charge of meanness and incapacity."

The above quotation requires little comment. The history of the French people since the introduction of the metric system, the progress of their industries, the extensive and intelligent use of the system by the poorest and most unlettered in the land are abundant refutation of Hazlitt's invective. Yet, when from the earliest days of the new weights and measures, Englishmen have been accustomed to reading such reports of the metric system, when they have, we imagine with incredible labor, mastered the intricacies of their system of coinage and learned to multiply and divide pounds, shillings, and pence it is not to be wondered at that they refuse to be dislodged from a position acquired by so many pains, in favor of one which appears seductively simple, but whose very simplicity is cause for suspicion! And to change would be to confess the inferiority and undesirable complication of their own system which anyone who understands the English character will readily appreciate the hopelessness of persuading an Englishman to do.

# GROWING MEDICINAL PLANTS IN AMERICA.[1]

By Allerton S. Cushman, Ph.D.,

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Modern warfare may be roughly divided into two distinct phases: one is destructive and the other reconstructive. There are no longer crucial battles which decide the issue of war as at Waterloo or Gettysburg, but there is instead one protracted and unceasing effort to destroy the enemy's life and property on the largest scale possible. Nevertheless, the reconstructive work must follow the destructive on an equally gigantic scale. Never before in the history of mankind has such organization existed for the first-aid and subsequent treatment of the sick and wounded, and never before has there been such concentrated human and animal suffering calling for alleviation.

It is a curious dispensation of Providence that man first found, and still to a very large extent depends for his remedial and anæsthetic agencies on the familiar herbs and weeds which grow wild about his woods, fields and hedgerows. The term "drug" includes all substances used as medicines, as well as those substances which may be misused as intoxicants or anæsthetics. Drugs may be mineral, such as the bromides, iodides, and chlorates of potassium, the mercurial, arsenical, and silver compounds and many others. In addition to these, modern medicine depends largely on the coal-tar derivatives, among which may be mentioned some of the more familiar, as, for instance, acetanilid, phenacetin, and the various salicylates, under such trade names as aspirin and salol, owned and exploited before the war exclusively by the Germans. The present paper, however, concerns itself particularly with the raw materials from which such medicinal agents as the alkaloids and glucosides are extracted. These are represented by morphine, cocaine, strychnine, atropine, quinine, digitalin, strophanthin, aloin, etc., which are extracted from crude drugs imported into this country from overseas.

[1] Presented at the stated meeting of the institute held Wednesday, April 17, 1918. Reprinted from the *Journal of the Franklin Institute,* September, 1918.

It is, however, more particularly the botanical drugs which can be grown under proper scientific control in the United States which we shall consider. Among these we find the following important medicinal plants: Aconite, belladonna, and stramonium, the principal source of atropine, digitalis (foxglove), cannabis indica or Indian hemp, the active principal of which is known in India as hashish, the properties of which the elder Dumas so beautifully misdescribes in "The Count of Monte Cristo."

FIG. 1. Planting belladonna seedlings at the rate of sixty to the minute.

Among our native medicinal plants we also use in fairly large quantity henbane, rhubarb, senna, gentian, golden seal (hydrastis), senega, mandrake, bloodroot, arnica; ajowan seeds, and monarda punctata, used in the manufacture of thymol, a specific in the treatment of the hookworm disease, and many others too numerous to mention. If a layman, unaccustomed to the study of such subjects, were to pick up one of the great New York commercial daily newspapers which quote prices in the drug markets and were to glance over the items quoted he would probably be very much astonished at the familiar herbs, roots, and flowers which are made a matter of

almost daily barter and sale, and manifold uses of which constitute some of the mysteries of our enormous patent medicine industry. There are warehouses in the heart of New York City filled with great bales of things familiar to our childhood days: cornsilk, daisy tops, red clover tops, laurel leaves, skunk cabbage, flagroot, burdock, dandelion, gentian, lily-of-the-valley, wintergreen, and many another of our old friends of the fields and woods. The inquirer might also be surprised to learn that these familiar things command a price

FIG. 2. A close up view of the two-man planter by means of which belladonna seedlings are set out.

varying from cents to dollars per pound and he might even solemnly determine to turn his newly acquired knowledge to profitable purposes and forthwith embark in the combination of business and pleasure of producing and purveying herbs and simples. Unfortunately, however, for this laudable ambition, it would soon become apparent that the labor involved, for instance, in gathering two bales of green corn silk or something else which shrinks to one bale on drying is quite inadequately paid for by the prices offered by the stony-hearted buyers in the New York market. In fact, it would

probably be learned that, although America produces more corn silk or something else than all of the rest of the world together, from time out of mind the baled corn silk or something else has been imported from overseas where child-labor laws are unknown and where people's wives, mothers, and grandmothers are more interested in acquiring a few extra pennies a day by working in the fields than they are in acquiring a vote.

Seriously speaking, the production of medicinal herbs in America

FIG. 3. A seven acre field of belladonna ready for the first harvest.

depends very largely on the labor cost, and can be made a profitable enterprise only when it is conducted on a scientific basis and on a sufficiently large scale to absorb the high cost of the labor involved in the tilling, planting, cultivating, harvesting, curing, and packing operations. At the same time, the drug grower faces a most uncertain and precarious market for his wares, for, although his drug plants are needed, the need is strictly limited, and the slightest overproduction is either entirely unsalable or salable at a price less than the cost of production.

A well-known authority on drug growing, Mr. H. C. Fuller, has

recently said in effect: "The cultivation and marketing of drugs must be done under an entirely different set of conditions than those obtaining in the growing and selling of vegetables. Much that has been published on the subject is misleading, and the idea that the ordinary farmer can successfully grow drug plants and produce a marketable article is ridiculous. It can be confidently asserted that if the ordinary farmer should undertake the growing of drug plants it would result in failure to him as well as discredit to the efforts of those who are specializing in the subject."

FIG. 4. Women harvesting belladonna leaves.

Dr. W. W. Stockberger, the Expert of the United States Department of Agriculture, in charge of drug and poisonous plant investigations, expresses the same fact in the following words:[2]

"If medicinal plant cultivation is to succeed in this country it must be placed on a sound commercial basis, and there are good reasons for believing that this end will not be attained by encouraging a large number of persons to engage in drug growing on a small scale." . . . "If the drug manufacturer is to become per-

[2] *The Druggists' Circular,* January 18, p. 5; *ibid.,* March 18, p. 106.

manently interested in medicinal plants produced in this country he must be assured of a fairly large and dependable source of supply. For this reliance must be placed upon well-equipped growers who have sufficient capital to carry on the enterprise effectively."

Still another writer on this subject has recently published the following comments:[3] "In the strictly pharmaceutical field the shortage of crude drugs has been felt more or less keenly since 1914, and much misinformation and little information of value have been

FIG. 5. Harvesting digitalis leaves.

circulated on the subject. Stocks of many crude drugs have been exhausted, and the cultivation of medicinal plants has not as yet assumed any great proportions in the United States. Those drugs which were obtained from Europe were not cultivated, but grew wild there. It was therefore a simple matter to have them gathered and prepared for market at comparatively small cost. The cultivation of medicinal plants in the United States requires expert labor, the production of artificial conditions of soil and moisture in order to provide as nearly as possible the conditions under which

[3] *Journal Franklin Institute*, vol. 185, No. 3, p. 435.

the plants grow in their native habitat, and considerable investment of money. Drug plants have been raised on an experimental scale by the government and in the drug gardens of various colleges, but it is a very different undertaking to raise them on a commercial scale. American growers of crude drugs were confronted with the necessity of increasing the value of the plants in order to overcome the high cost of cultivation. It was soon found that cross-pollination would not produce plants containing more active constituents

FIG. 6. A field of cannabis.

than they do normally, but by careful selection of seed it has been possible to increase the amount of active constituents in such plants as belladonna, digitalis, etc., to three of four times what the Pharmacopœia requires. Furthermore, advanced methods of harvesting these plants have made it possible to secure three or four harvestings in one season, whereas in former years one or two was the limit."

The experience gained by the author in the production of certain drug plants extending over the past three years confirms the statements of the experts quoted above. The fact is very clearly brought out that the so-called "backyard" movement, however

much it may stimulate vegetable gardening and poultry raising, is not applicable to the growing of medicinal plants. The U. S. P. requirement for dry belladonna herb or leaf calls for an assay showing a content of not less than 0.3 per cent. atropine alkaloid. Any substantial quantity of active constituents in excess of this prescribed minimum should, if the producer is aware of it, be credited in the price paid by the consumer. The small producer can have no knowledge of the assay value of his product unless he employs the services

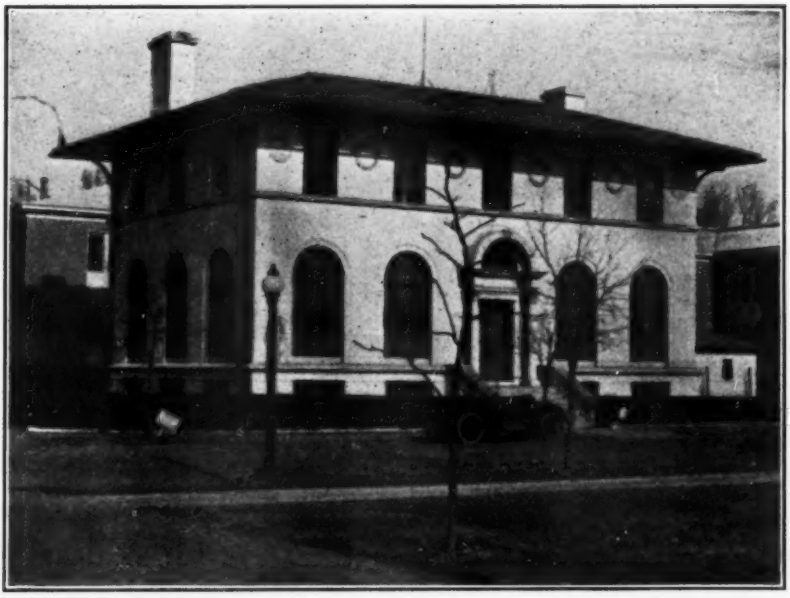

FIG. 7. The Institute of Industrial Research, Washington, D. C., where the drug plants are analyzed and tested.

of a chemical laboratory. Such chemical assays require special highly paid experts in order to obtain accurate results, and the cost of such service is naturally high. In the opinion of the writer, unless a producer is able to hold his belladonna to an assay value at least twice as strong as the U. S. P. requirement it would not be worth producing at all under American conditions. Such high-potency crude drugs can be obtained only by the application to the problem of trained scientific knowledge. Plant breeding through seed selection and a knowledge of just the day to harvest when the

alkaloidal content is at the maximum, together with proper control of the drying operations, constitute a large part of the secret of success. All this necessarily hangs upon the results of laboratory investigation, which must go on hand in hand with the agricultural operations. The author and his associates have produced belladonna in bulk running almost one per cent. alkaloid-atropin.

Other important medicinal crops, such as digitalis and cannabis, present a special problem, inasmuch as the active constituents are

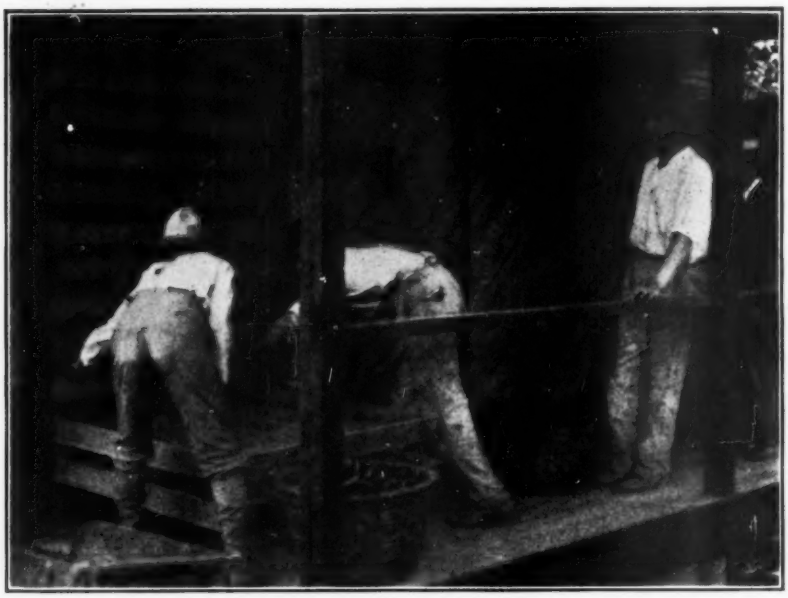

FIG. 8. Preparing to fill the dryer where the herbs and roots are cured.

not determinable by chemical assay, but depend upon certain specific physiological tests which require the services of another group of trained specialists.

In marketing crude drugs the pharmacopœial requirements must be met, no matter how irrational these may be. The requirement on cannabis calls for the dried flowering tops of unfertilized pistillate of female plants only. This specification requires that before the male plants pollinate experts must go over the entire crop, plant by plant, and distinguish and destroy every male individual. Immediately the visible crop shrinks approximately fifty per cent., and

also adds to its cost of production the cost of this wholesale weeding operation. This requirement also necessitates the seed gardens being remote enough from the main crop to prevent wind-blown pollen from reaching the female survivors. In order to test the necessity for this requirement, the author, in coöperation with Mr. H. C. Fuller, gathered from the seed gardens flowering male tops, which were dried, powdered, and bottled. This sample, together with a pharmacopœial sample bearing distinguishing numbers but no other information, was sent to the physiological laboratory of the Harvard Medical School. The report showed the male sample was the more physiologically active of the two. Although the pharmacopœial requirement is probably a survival of some superstition originating in India, the drug-plant grower is held rigidly to it, and it is extremely unlikely that any buyer would purchase the crude drug in the powdered form, as the dried flowers must be present so that inspection will detect the presence of male plants. If such specifications are annoying to the commercial drug grower, they would be found intolerable by an ordinary farmer who might otherwise feel inclined to undertake the production of this special crop.

All medicinal plants are intensely poisonous to animals, but curiously enough, most of them are very attractive to predatory insects. Possibly insects share with man a weakness for certain things that would better be let alone. However this may be, the author has determined by actual experiment that the flea beetle consumes about five per cent. of every crop of belladonna grown, in spite of the most liberal use of insecticides and agricultural spraying machinery.

Henbane, the crude drug from which hyoscyamine is made, sells at about four dollars a pound on the dry basis, and is worth it, owing to the eagerness with which insects appear to lie in wait for every green shoot as it appears. In the course of the author's experience potatoes were grown in the neighborhood of henbane, in the hope thot it would act the part of a decoy crop. Unfortunately, however, the potato beetles preferred the henbane, and—if we may be permitted to drop into the vernacular—returned to their own homes only after all the other places were shut up.

Among the medicinal plants which the author and his associates have attempted to grow commercially in Virginia and Maryland, many of them successfully, are belladonna, digitalis, cannabis, sage, hydrastis, ginseng, stramonium, monarda punctata, pinkroot, valerian, senega, colchicum, etc. Of these, the first two have to be propagated

in a greenhouse during the winter in order that the plants, when set out in the field, will be large and vigorous enough to cope with the ravages of insects and crowding out by weeds. The greenhouse soil has to be especially sterilized to prevent the spread of a special fungoid root-rot disease to which belladonna is especially susceptible and which follows the seedlings from the greenhouse to the open fields. During one season the writer lost over fifty per cent. of his belladonna crop, due to root-rot. So suddenly did the disease show iteslf that on one day the bushy plants, about two feet high, were flourishing in the field and the next day were found wilted down and dying. The roots of belladonna are rich in atropine and are usually dug up and sold after a succession of leaf crops have been gathered, so that the loss from root-rot is most discouraging and baffling.

Ginseng and hydrastis (golden seal) grow in leafy, shady woods and are much appreciated by field mice, which seem to feel that the crops are being grown for their exclusive benefit. Moles, although they do not appear to eat the roots, are most destructive and prefer to burrow along a line of valuable plants rather than go anywhere else. Ginseng is not used as a drug in any country except China, so, if grown, it is only for export. It is doubtful if, under present conditions, its cultivation can be carried on profitably in this country except by specialists in this crop.

This paper has not attempted to discuss drugs or drug growing in their technical aspects, but merely describes a few of the conditions and difficulties encountered by a group of associates who entered the field with no expectation of making large profits, but with the patriotic purpose of demonstrating, if possible, that American methods were capable of making us independent of central Europe with respect to some very necessary medicinals.

# NUCLEIC ACID AND ITS ANALYTICAL EXAMINATION.[1]

By A. Chaston Chapman, F.I.C.

During recent years nucleic acid and certain of the metallic nucleates have found somewhat wide and increasing application in medicine, and particularly in connection with surgical practice. At the outbreak of war, these substances were obtained chiefly from Germany and America, and so far as I am aware were not manufactured at all in this country. A number of urgent enquiries having been received from France and elsewhere, the Pharmaco-Chemical Products Company, Ltd., suggested to me that I should undertake the investigation of this matter with the object of devising methods for the manufacture of pure nucleic acid and its derivatives on a large scale. Yeast was obviously the most convenient raw material, and for more than a year the above-mentioned company have been manufacturing considerable quantities of pure yeast-nucleic acid and its compounds.

It will be obvious that, in the prosecution of this work, it was necessary to have methods for examining the products obtained and to establish analytical *criteria* of purity. The production of pure nucleic acid on a large scale presents many difficulties, the two chief ones being the complete removal of protein and the prevention of the contamination of the acid with the products of its own decomposition. This will be at once apparent when it is remembered that nucleic acid results from the breaking-down of the nucleo-proteins of the cell nuclei on the one hand, and that, on the other, it yields, as the result of further hydrolytic change, a number of complex nucleosides and bases, together with phosphoric acid and the carbohydrate *d*-ribose. The conditions for hydrolysis have therefore to be very exactly determined and very strictly observed in practice.

Up to the present two nucleic acids have been very fully studied, the one derived from yeast, the other from the thymus gland. Whether these two acids represent typical members of two sharply defined groups, or whether all nucleic acids are identical with the one or the other, is at present a little doubtful. The latter view is, however, the one more generally held, and the nucleic acid from yeast is frequently known by the more comprehensive term "plant-

[1] From *The Analyst*, July, 1918.

nucleic acid." It is with this plant nucleic acid that the present paper chiefly deals.

The following statement shows at a glance the chief products of hydrolysis of these two nucleic acids, and at the same time affords an insight into their respective chemical constitutions:

*Plant Origin.*—Guanine, adenine, cytosine, uracil, *d*-ribose (pentose), phosphoric acid.

*Animal Origin.*—Guanine, adenine, cytosine, thymine, lævulinic acid (from a hexose), phosphoric acid.

Plant nucleic acid is a white friable substance devoid of odor or taste, and having the formula $C_{38}H_{50}O_{29}N_{15}P_4$. It is practically insoluble in water, but dissolves readily in solutions of alkaline acetates. It is also readily soluble in solutions of the alkalies forming the soluble alkaline salts. From these solutions a few drops of hydrochloric acid precipitate the nucleic acid in a dense curdy form, which dissolves completely on the addition of a large excess of the acid.

When acetic acid is added to a solution of the sodium salt, the acid is partly precipitated, but no precipitate is formed on the addition of any acid in the presence of a sufficient quantity of alkaline acetate.

When added to a solution of sodium nucleate, a solution of copper acetate acidified with acetic acid gives a bulky greenish-blue precipitate.

Calcium chloride in excess in the presence of a few drops of acetic acid gives a white precipitate at first flocculent, quickly becoming more granular.

Silver nitrate, when added in considerable excess to a fairly strong and neutral solution of sodium nucleate, gives a white gelatinous precipitate. On the addition of a little sodium chloride this dissolves, forming an opaque colloidal solution. One drop of hydrochloric acid added to this precipitates the silver as chloride.

Solutions of sodium nucleate in water exhibit a marked tendency to gelatinize, and, if sufficiently strong, set to a jelly.

The above reactions, coupled with the recognition of guanine and adenine (which are the most easily isolated and best defined of the bases formed on hydrolysis), suffice for the identification of nucleic acid, when it exists in a fairly pure condition.

For the hydrolysis of nucleic acid 10 grm. of the acid (or a

larger quantity if available) are heated in a boiling water-bath for two hours with 40 Cc. of 10 per cent. sulphuric acid (or a proportionately larger quantity if more than 10 Gm. are taken) in a small flask fitted with an air condenser. At the end of this time strong ammonia is added to the hot solution in the flask until the liquid contains an excess of about 2 per cent. The guanine is precipitated in a granular form, the adenine remaining in solution. After filtering and washing with 1 per cent. ammonia, the guanine is dissolved in the smallest possible quantity of dilute sulphuric acid, decolorized if necessary by means of a little animal charcoal, and the base precipitated again from the colorless solution by the addition of an excess of ammonia. The purified base may then be converted into the hydrochloride, which crystallizes very readily and may be easily identified by the application of any of the well-known tests. The ammoniacal filtrate from the guanine, together with the ammoniacal washings, is acidified with sulphuric acid, heated to boiling, and the adenine precipitated as a cuprous compound by the addition of a 10 per cent. solution of copper sulphate. Inasmuch as the solution contains the carbohydrate ribose, it is not necessary to add sodium bisulphite for the purpose of reducing the cupric compound. The adenine-copper compound is suspended in hot water, decomposed with sulphuretted hydrogen, and the filtrate from the copper sulphide evaporated to dryness on the water-bath. The residue, consisting of nearly pure adenine, is dissolved in 5 per cent. of sulphuric acid, and the adenine sulphate, which is readily soluble in hot, but very slightly soluble in cold water, allowed to crystallize. The usual tests can then be applied.

The following is an outline of the procedure to be adopted for the examination of nucleic acid, with the object of ascertaining its purity and quality.

The acid should be white or at the most have a very faint buff color. It should be completely soluble in an aqueous solution of sodium acetate or in dilute solutions of ammonia or of sodium or potassium hydroxides. The solutions in these reagents should be bright and almost colorless. When a few drops of hydrochloric acid are added to a solution of the sodium salt in water, the acid should be precipitated as a white curdy substance, and on the further addition of a large excess of the hydrochloric acid this should dissolve completely. An aqueous solution of the sodium salt should give with

cupric acetate, calcium chloride and silver nitrate the reactions described above.

### Tests for the Absence of Protein.

*Biuret Reaction.*—A solution of the acid in an excess of caustic soda should give, on the addition of one or two drops of dilute copper sulphate solution, a greenish-blue color with at the most a faint tinge of purple. This test is quite sufficient, but occasionally the following test is applied:

A 5 per cent. solution of nucleic acid in a small excess of ammonia, when heated in a bath at 105° C., should give at the most a slight turbidity.

In connection with these tests, it may be pointed out that the removal of the last traces of protein matter from nucleic acid involves a very troublesome series of treatments, and that acid of high commercial quality will usually give an indication of the presence of traces of protein when subjected to the above tests. The second of the above tests is the more severe, inasmuch as an amount of protein equal to not more than 0.1 or 0.2 per cent. (expressed on the acid) gives a very appreciable volume of precipitate.

*Inorganic Phosphate.*—To a solution of the acid in excess of ammonium or sodium acetate a few drops of acetic acid are added, and then a little uranium acetate. A flocculent precipitate is formed, which in the absence of more than a trace of inorganic phosphate should dissolve completely on boiling. A considerable excess of alkaline acetate is necessary in this test.

### Estimation of Nitrogen and Organic Phosphorus.

*Nitrogen.*—This is estimated by the Kjeldahl method in the ordinary way.

*Phosphorus.*—A weighed quantity of the acid is fused with six times its weight of sodium carbonate containing 10 per cent. of potassium nitrate. The fused mass is taken up with water, and in this solution the phosphoric acid is estimated either by the molybdate method or by direct precipitation with magnesia mixture in the presence of a little ammonium citrate.

It will be seen that the formula given above corresponds with 16.1 per cent. of nitrogen and 9.5 per cent. of phosphorus.

Commercial nucleic acid of good quality ought to contain not

much less than 15 per cent. of nitrogen and 9 per cent. of organic phosphorus (expressed on the moisture-free sample). The examination of nucleic acid should always include these two items, and the ratio of the percentage of organic phosphorus to that of nitrogen is one of the best *criteria* of the purity of the acid, since, if this ratio (1 : 1.7) is approximately correct, the presence of any appreciable proportion of the products of hydrolysis is excluded.

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## THE MANUFACTURE OF CHLORAMINE-T.[1]

By J. K. H. Inglis.

Although two years have elapsed since Dakin showed the value of chloramine-T as an antiseptic, no detailed account of the method of manufacture has yet been published. The drug has shown itself of great value in cases of cerebrospinal meningitis, diphtheria, etc., and after a trial of a small specimen which I had made, I was asked to supervise the manufacture of a regular supply for the military camps in New Zealand, it having been found impossible to procure it outside the Dominion.

In Dakin's work the starting point for the preparation was *p*-toluenesulphonic chloride, obtained as a by-broduct in the manufacture of saccharin. No such material being available in New Zealand, details had to be worked out for the manufacture from toluene itself, and these details form the material for this paper.

*Sulphonation.*—The sulphonation of toluene with concentrated sulphuric acid leads to the formation of the three possible monosulphonic acids; but the higher the temperature the larger the proportion of *p*-acid (Ber., 1911, p. 2504), the highest proportion being 70 to 80 per cent. The price of sulphuric acid being relatively high in New Zealand, I found it best to use two parts by weight of sulphuric acid (sp. gr. 1.84) to one part of toluene (approximately equal volumes) and to carry out the sulphonation at the boiling point of toluene. 250 Cc. of sulphuric acid (1.84) is heated to 110° C. by immersing the reaction flask in a heated paraffin bath, and then 250 Cc. of hot toluene is added, the whole being very vigorously stirred with a glass circulating stirrer. The efficiency of the stirring

[1] Reprinted from *Jour. of the Soc. of Chemical Industry*, September, 1918.

is very important, as upon it depends the time necessary to complete the sulphonation. This reaction was carried out in a flask fitted with a reflux condenser, and only a small loss of toluene vapour took place, sulphonation being complete in about thirty minutes with very little charring. Under these conditions about 75 per cent. of the toluene is converted into the *p*-sulphonic acid, the remainder being a mixture of *o*- and *m*-acids. If this mixture of acids was isolated, converted into dry sodium salts, and treated with phosphorous pentachloride, the *p*-chloride could be obtained; but as the other chlorides would be useless there would be a considerable waste of material. We therefore made use of Lange's discovery (Ger. Pat. 57, 391) that if water is added so that the mother liquid consists of only 66 per cent. sulphuric acid, then on cooling, the crystals that separate consist only of the *para*-acid which separates almost completely—the mother liquid retaining the *o*- and *m*-isomers in solution. In order to carry this out, 45 Cc. of water is added to the reaction mixture after sulphonation as above and the liquid poured out and cooled. The liquid rapidly crystallises and sets to a crystalline cake, and on filtering over an asbestos mat (as in a Gooch crucible) nearly the whole of the mother liquid can be drained away, leaving a white crystalline mass which proves to contain only small amounts of *o*- and *m*-impurities. The crystals that separate appear to be the monohydrate, $C_7H_7SO_3H$, $H_2O$, and correspond to about 75 per cent. of the toluene taken. Hence about 25 per cent. of the toluene is either lost as vapour or is contained in the mother liquor in the form of the *o*- and *m*-acids. The separation by crystallisation is, however, not very sharp, and the mother liquid on standing continually deposits further crops, which, however, are nearly free from the *para*-acid.

The *o*- and *m*-acids being useless to us, experiments were made by Mr. C. L. Carter at my suggestion, to see how completely the toluene could be recovered by the action of superheated steam. It was found that if the liquor were heated to about 170° and then a brisk current of steam at 200° were blown through it the bulk of the toluene was rapidly evolved, the distillate containing at first as much as 20 per cent. toluene. When the percentage fell below 5 per cent. the operation was stopped, as further continuance was hardly profitable (Armstrong, *J. Chem. Soc.*, 1884, 45, 148). The total amount thus recovered was about 14 per cent., leaving 11 per cent.

not accounted for. Part of this is lost by evaporation during mixing and subsequent sulphonation, and a small part is left in the sulphuric acid. Probably most of the remainder is lost by evaporation *in vacuo* during the filtration of the crude acid.

The cake of crude *p*-acid is dissolved in water, slightly more than enough calcium carbonate is added to precipitate the sulphuric acid as calclum sulphate, and the still acid liquid is filtrated. It is then nearly neutralized with caustic soda, made distinctly alkaline with sodium carbonate, boiled, and again filtered. It is important to remove the calcium as completely as possible, as it may become a troublesome impurity in the later stages. This method gives a solution containing only sodium sulphonate and sodium carbonate, and on acidifying with hydrochloric acid and evaporating to dryness there remains a pure white salt consisting of the required sodium sulphonate with a trace of sodium chloride. The sulphonate is so soluble in water that this seems to be the best method of preparation.

*Preparation of the Sulphonic Chloride.*—This can easily be prepared by heating together on the water bath approximately equal weights of sodium salt (dried at 140° C.) (191 Gm.) and phosphorus pentachloride (208.5 Gm.). In this case the reaction takes place very rapidly and easily and a large amount of phosphorous oxychloride is obtained. Mr. C. S. Hicks, working in my laboratory, found, however, that the oxychloride itself can be used according to the equation, $2XSO_3Na + POCl_3 = 2XSO_2Cl + NaPO_3 + NaCl$, and he obtained a 76 per cent. yield. Hence if less than half the weight of pentachloride be taken and the mixture be heated some hours on the water-bath under reflux condenser the following reaction takes place: $3XSO_3Na + PCl_5 = 3XSO_2Cl + 2NaCl + NaPO_3$. The proportions of salt and pentachloride according to this equation are 573 to 208.5, or 2–3/4 to 1; but the reaction is very slow towards the end as the mass becomes too solid and the yield is apt to decrease. This trouble might be avoided by using the theoretical proportion of pentachloride and sufficient oxychloride, which should then be recovered unchanged. An experimental trial of this gave 92 per cent. yield but the oxychloride was not recoverable. We therefore use 2 parts of sodium salt for each part of pentachloride and the action then completes itself more easily and only small amounts of oxychloride are left over—the reaction being

allowed to go on over night under reflux condenser on a water-bath. The oxychloride is then distilled off *in vacuo* and the residue put into cold water. The sulphonic chloride is the only part insoluble and is separated by filtration: a small amount of oily impurity (*o*- and *m*-sulphonic chlorides) can be pressed out from the solid cake. The yield is nearly quantitative, 96–99 per cent. The solid sulphonic chloride still contains small amounts of *o*- and *m*-impurities, but these are gradually eliminated in the later stages.

*Preparation of Sulphonamide.*—This operation, though quite simple in theory, causes a certain amount of trouble without special apparatus. The alternative methods are treatment with ammonium carbonate on the water-bath and treatment with strong ammonia solution. The latter method, if properly controlled, is decidedly the more satisfactory. If the sulphonic chloride is ground to a fine powder and concentrated ammonia is poured upon it, a violent reaction begins almost at once and the liquid boils. In this way considerable amounts of ammonia are driven off and the action is apt to be incomplete. We had some difficulty in procuring vessels in which the reaction could be conveniently carried out under pressure, and owing to the impossibility of getting special vessels made which would stand the action of a hot mixture of ammonia and ammonium chloride, we used stoneware ginger-beer bottles which had a screw stopper with a rubber seating. 100 Gm. of sulphonic chloride could be placed in each, 100 Cc. of 0.880 ammonia quickly added and the stopper screwed in firmly. On shaking vigorously the action began, and as soon as the bottle became too hot to hold it was placed in cold water. No mishaps occurred and the yield was excellent, the liquid only requiring filtering and the residue washing with cold water. The mother liquors on evaporation give small amounts of the *m*-amide but very little else besides the ammonium chloride. Under these conditions about half the ammonia taken is actually used and on a large scale the unchanged ammonia could be recovered by boiling the liquors. The yield of *para*-sulphonamide is 94–97 per cent.

*Preparation of Chloramine-T.*—The conditions for the conversion of amide to chloramine were given in detail by Dakin, one mol. of amide being dissolved in 1.2 mols. of sodium hypochlorite of definite concentration and the chloramine then precipitated by the addition of strong brine. At first his actual proportions were used, but it was found to be unnecessary to use brine. If the amide is

dissolved in a warm, strongly alkaline solution of sodium hypochlorite of concentration 1.3 to 2.0 N, a large crop of chloramine is formed on cooling and the remainder can easily be obtained on evaporation. It is very important to have a decided excess of caustic soda, and for each mol. of amide we usually take 1.05 to 1.1 mols. of hypochlorite and 1 mol. of sodium hydroxide. The preparation of the hypochlorite is of course straightforward. Owing, however, to the cost of acids in New Zealand and to there being no electrolytic source of chlorine, we found it most convenient and cheapest to use bleaching powder as the starting point. The crude chloramine-T obtained in this way is contaminated with sodium chloride; but even the crude crystals on drying contain 92–95 per cent. of chloramine. The substance can be easily purified by recrystallization from water. If dissolved in twice its weight of hot water, a large proportion can be obtained in the pure form (over 98 per cent.) on cooling. The final filtration is apt to be troublesome; the crystals do not pack well on the filter and it is therefore difficult to remove the mother liquid completely. If, however, the cooling is carried out rapidly without stirring a different shape of crystal is obtained which filters much more readily. It is thus possible, working with large quantities, to get a product of over 99 per cent. purity.

*Utilization of By-products.*—In the sulphonation as described most of the toluene is used, but half the sulphuric acid taken is contained in the mother liquors after removal of the toluene by superheated steam. At first it was hoped that it would be possible to recover the acid in the pure state by distillation and use it over again; but there is always some charring and the impurities remaining make it comparatively useless. It contains 34 per cent. of water. In the remaining stages of preparing the sulphonate the by-products are small in quantity and comparatively valueless. Some lime or calcium carbonate is used and converted into sulphate, but the quantity is very small. In the preparation of the sulphonic chloride the by-products are sodium chloride and sodium *ortho-* and *meta*-phosphate. It would probably be worth while to utilize the latter on the large scale but out experiments are incomplete. In the preparation of the sulphonamide the chief by-products are ammonium chloride and excess of ammonia. The former can be easily recovered and the ammonia could be made use of with suitable apparatus.

In the preparation of hypochlorite and of chloramine, the by-products are calcium carbonate—a nearly pure precipitate—and a liquor consisting of sodium chloride and hydroxide. No doubt use could be made of this liquor but we have made no attempt in this direction. The above results have been obtained under laboratory conditions making some pounds of chloramine per week. Owing to lack of filtering apparatus and other labor-saving devices we have not made experiments on a still larger scale; but our experiments have always been made with a view to their application to large-scale operations and we have every reason to believe that they would not fail in commercial practice.

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## EMETINE: NEW PREPARATIONS.[1]

At a meeting of the Chemical Society early in the year, F. L. Pyman described a stereoisomeride of emetine known as *Iso-emetine.* Physiological tests by H. H. Dale showed that this substance has about half the toxicity of emetine when given to rabbits intravenously. Clinical reports by G. C. Low, however, show that although it is well tolerated by man it does not appear to have any curative effect in amoebic dysentery.

An "emetine adsorption product," devised by Dale, but the exact composition of which is not stated, is reported on by R. Donaldson *et al.*,[2] who give it an extensive trial side by side with emetine bismuth iodide. Their results show that these two substances are of equal potency as regards rendering the stools negative, and that both are superior to emetine administered subcutaneously. Emetine bismuth iodide is handicapped by its disturbing effect on the stomach, and is inferior to the emetine adsorption product, which is well tolerated. The cases examined appear to show that not more than 50 to 60 per cent. may be regarded as possible cures after one course of twelve doses, therefore the minimum course of twelve doses should be increased, and the emetine adsorption product should be used instead of any other preparation. Of nine cases treated only one had vomiting, in two cases there was slight enfeeblement of the heart's action, and in four there was looseness of the bowels.

[1] Reprinted from *The Prescriber,* October, 1918.
[2] *Practitioner,* 1918, 101, I; July.

## THE NEWLY ELECTED OFFICERS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The tellers have announced the results of the election for officers of the Association that has been held by mail. Those elected to preside over the destiny of the Association during the association year 1919–1920 are: President, Prof. L. E. Sayre; First Vice-President, Prof. Theodore J. Bradley; Second Vice-President, Harry Whitehouse; Third Vice-President, Prof. E. Fullerton Cook; Members of the Council for three years, Dr. James H. Beal, Prof. Charles H. La Wall, Samuel L. Hilton.

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## CURRENT LITERATURE.

### SCIENTIFIC AND TECHNICAL ABSTRACTS.

ADULTERANT OF STRAMONIUM LEAVES.—A large consignment of stramonium leaves recently sent from Spain and France was found on examination to consist almost entirely of the leaves of *Xanthium macrocarpum* DC., a plant widely distributed, especially in the Mediterranean region. Although the spiny fruiting capitulum somewhat resembles the fruit of stramonium, the leaves are easily distinguished by their smaller size, yellowish-green color, and harsh hairs occuring on the lamina. Under the microscope three forms of hairs are to be seen, two protective and one glandular. Of the protective hairs one form is short and lignified, the other longer; the glandular hairs are characterized by the rosettes of calcium oxalate in some of the cells. Rosettes of calcium oxalate are also to be found in the mesophyle, but they are much smaller and less numerous than those of stramonium. A transverse section of the midrib exhibits six bundles, whereas in stramonium the bundle is undivided. The leaves of *X. Strumarium* L., have also been found in stramonium leaves. (*Pharm. Journ.*, 1901, p. 326.)—(P. Guerin, *L'Union Pharm.* Through the *Pharmaceutical Journal* and *Pharmacist.*)

STORAX ASSAY.—Van Itallie and Lemkes suggest the following method for determining the cinnamic acid in storax: Boil 1 Gm. with 20 Cc. of *N*/2 alcoholic solution of potash for one hour under a

reflux condenser, evaporate to dryness and redissolve in 25 Cc. of water. Shake this solution out with ether, wash the ether with water and return the washings; dilute to about 950 Cc., add 10 Cc. of dilute sulphuric acid, and make the volume up to 1,000 Cc. Mix 100 Cc. of this with 10 Cc. of $N/10$ potassium bromate solution, 1 Gm. of potassium bromide, and 5 Cc. of sulphuric acid. After 15 minutes add 1 Gm. of potassium iodide, stand for 5 minutes, and titrate with $N/10$ sodium thiosulphate. Not more than 6.5 Cc. should be required. 1 Cc. $N/10$ potassium bromate solution corresponds to 0.00/4 Gm. of cinnamic acid. (*Schweiz. Apotheker Ztg.*, 1918, p. 286. Through the *Pharmaceutical Journal* and *Pharmacist.*)

Classification of Bacteria as to Diastase Production.—During the last two years in the Dairy Bacteriology Laboratory of the University of Illinois the use of potato slants for the determination of diastase production by bacteria has been replaced by a simple plate method as follows: A starch agar is made by adding 0.2 per cent. of water-soluble starch to the regular plain agar. This starch agar can be sterilized in the autoclave along with other mediums. Some hydrolysis takes place, but not enough to interfere with the test. The agar is poured into Petri dishes and allowed to cool, when a stroke 2 inches long is made with a loopful of an agar slant growth of the organism to be tested. The plates are incubated for two days at 37° C. and five days at 20° C., after which they are flooded with a saturated solution of iodine in 50 per cent. alcohol. A clear area about the stroke averaging more than 2 mm. in width classifies the diastatic action as strong, while a width of 2 mm. or less marks it as feeble and the absence of a halo as absent. (P. W. Allen, Urbana, Ill. *Journal of Bacteriology,* Baltimore. Reprinted from *The Journal of the American Medical Association.*)

Urine Staining Technic.—Minerbi heats the isolated urine sediment with human blood serum or egg albumin, both of which coagulate under the action of fixation measures. Then when the May-Grunwald-Giemsa stain is applied, the background is homogeneous and colorless, and the preparation is exceptionally instructive in every respect. After centrifugating the urine, all the fluid is decanted except one or two drops. Then a droplet of egg albumin is taken up on a platinum loop and the loop is plunged into the sediment and agitated to mix it, with care not to cause produc-

tion of bubbles. Then the mouth of the tube is held slanting on an object glass and with the platinum loop a droplet is spread all over the object glass, and two other slides are prepared in the same way. Before drawing out the sediment, the loop is singed to be sure that no undissolved albumin is sticking to it. He regards the method as extremely practical and instructive. His first publication on the advantages of impregnation of the sediment with human serum date from 1914. (C. Minerbe. *Rivista Critica di Clinica Medica,* Florence, through *The Journal of the American Medical Association.*)

EUPATORIUM GLUTINOSUM LAM. SUBSTITUTED FOR MATICO N. F.—Examination of importations of "matico leaves" (*Piper angustifolium* Ruiz et Pavon) has disclosed that in one instance the leaves of *Eupatorium glutinosum* Lam. have been substituted for the true material. *Piper angustifolium* has alternate leaves, which have a finely crenulate margin, unequal subcordate base, a finely bullate upper surface, and prominent venation below, and have no glandular hairs; whereas *Eupatorium glutinosum* has opposite leaves, which have a serrate margin, cordate base, coarsely bullate upper surface, and numerous glandular hairs. The flowers, which occur occasionally in samples of the leaves, consist of a spike in the case of matico and of a cymose paniculate composite head in the case of *Eupatorium glutinosum.* The department will recommend the detention of shipments of "matico leaves" found to consist in whole or in part of the leaves of *Eupatorium glutinosum.—Service and Regulatory Announcements U. S. Department of Agriculture, No. 23.*

GREEK SAGE AND SPANISH SAGE SUBSTITUTED FOR SAGE (SALVIA OFFICINALIS).—Examination by the bureau of commercial samples of "sage" has disclosed that in some instances the samples were not obtained from *Salvia officinalis* L., but consisted of the leaves of Greek sage, *Salvia triloba* L., and Spanish sage, *Salvia lavandulæfolia* Vahl. These forms, while very closely related to true sage, have certain differences in appearance and flavor, and are well recognized by the trade as distinct forms. Greek sage may be distinguished from true sage by the usually broader, shorter, thicker, entire leaves, short petioles, and by their more wooly appearance. Spanish sage may be distinguished by its smoother, considerably smaller, entire leaves and relatively long petioles. Neither Greek sage nor Spanish

sage possesses the crenulate edge and the strong venation characteristic of true sage. The department is of the opinion that the term "sage," without any qualifications, applies only to material obtained from *Salvia officinalis,* and should not be used for material obtained from other related species nor for mixtures of other species with it. Material obtained from *Salvia triloba* should be labeled "Greek sage"; material from *Salvia lavandulæfolia* should be labeled "Spanish sage." Mixtures of these forms should be sold only under an appropriate label.—*Service and Regulatory Announcements U. S. Department of Agriculture, No. 23.*

Macrotomia Cephalotes D. C. Substituted for Alkanet Root (Alkanna Tinctoria Tausch.).—Examination of samples of "alkanet root" (*Alkanna tinctoria* Tausch.) has disclosed that in one instance the root of *Macrotomia cephalotes* D. C. has been substituted for the true material. *Macrotomia cephalotes* is very much larger than the genuine alkanet; it occurs in pieces from 20 to 40 centimeters long and from 2 to 5 centimeters thick, whereas alkanet is about 1 to 1.5 centimeters in diameter and is usually 10 to 15 centimeters in length. It is black-violet in color and somewhat metallic in appearance, whereas alkanet is of a dull maroon color. It has a distinctly spiral twist, resembling a twist of tobacco, whereas alkanet is only slightly twisted. Preliminary experiments made in this bureau indicate that it contains considerable amounts of a coloring principle resembling that of alkanet. The department will raise no objection to its importation if properly invoiced, labeled, and sold.—*Service and Regulatory Announcements U. S. Department of Agriculture, No. 23.*

Bombay or Indian Coriander.—Examination of importations of "coriander seed" (*Coriandrum sativum* L.) has disclosed that in some instances they have consisted of fruits differing in physical appearance from the Pharmacopœial description. The fruits are oval instead of spherical and not infrequently yield less volatile oil than the Pharmacopœial article. The product appears in the trade as "Bombay" or "Indian" coriander and appears to have value. The department will not object to the importation of Bombay or Indian coriander if invoiced, labeled, and sold as such, provided that any deficiency in volatile oil be indicated.—*Service and Regulatory Announcements U. S. Department of Agriculture, No. 23.*

PIPTOSTEGIA PISONIS MART. SUBSTITUTED FOR JALAP U. S. P.—Examinations of importations of "jalap root" (*Exogonium purga* (Wenderoth) Benth.) have disclosed that in some instances the root of *Piptostegia pisonis* Mart. has been substituted for the true material. It occurs in commerce in the form of transverse circular or oval sections, varying from about 3 to 8 centimeters in diameter and from about 0.3 to 0.8 centimeter in thickness, whereas jalap generally occurs in fusiform irregularly ovoid or pyriform tuberous roots, the upper end more or less rounded, the lower end slightly tapering, the roots varying from 4 to 15 centimeters in length and from 12 to 60 millimeters in diameter. The pieces of *Piptostegia pisonis* are marked with several concentric rings, aside from the pale grayish-brown tint and the presence of numerous dots of translucent pale resin on the surface, bear considerable resemblance to white bryony root. Preliminary experiments with resin isolated from the root in this bureau indicate that the material has purgative properties. The department will raise no objection to the importation of *Piptostegia pisonis*, provided it is properly invoiced, labeled, and sold. In releasing such goods, however, the department will take such precautions or impose such conditions as seem necessary to prevent its sale as jalap U. S. P.—*Service and Regulatory Announcements U. S. Department of Agriculture, No. 23.*

STROPHANTHUS SARMENTOSUS SUBSTITUTED FOR STROPHANTHUS SEED (STROPHANTHUS HISPIDUS).—Examination of importations of "Strophanthus seed" (*Strophanthus hispidus* P.DC.) has disclosed that in some instances the seeds of *Strophanthus sarmentosus* P.DC. have been substituted partially or wholly for the true material. The embryo of *Strophanthus hispidus* contains no crystals of calcium oxalate and gives a green color when treated with 80 per cent. sulphuric acid, whereas the embryo of *Strophanthus sarmentosus* has abundant crystals of calcium oxalate, and gives a red color when treated with 80 per cent. sulphuric acid. The department will recommend the detention of any shipment of *Strophanthus hispidus* found to consist in whole or in part of the seeds of *Strophanthus sarmentosus*. There is little reliable data available regarding the physiological activity of this species.—*Service and Regulatory Announcement U. S. Department of Agriculture, No. 23.*

ACONITUM CHASMANTHUM STAPF. SUBSTITUTED FOR ACONITE U. S. P.—Examination of importations of "aconite" has disclosed that in one instance the root of *Aconitum chasmanthum* Stapf. has been substituted for the true material. The root of *Aconitum chasmanthum* is generally smaller than that of *Aconitum napellus*, about 2 centimeters long and about 0.75 centimeter in diameter; it is less wrinkled and the rootlet stubs are usually clustered at the basal end. Its fracture is lighter in color and its texture less tough and resinous. The department will recommend the detention of any shipment of aconite root found to consist in whole or in part of the roots of *Aconitum chasmanthum*. In releasing such goods, the department will take such precautions or impose such conditions as seem necessary to prevent their sale as aconite U. S. P.—*Service and Regulatory Announcement U. S. Department of Agriculture, No. 23.*

## MEDICAL, PHARMACEUTICAL AND DISPENSING NOTES.

CUTANEOUS IRRITATION BY MUSTARD OIL AS INFLUENCED BY VARIOUS SOLVENTS.—Sollman says that olive oil and other good solvents for mustard oil hinder its penetration into the skin. The greatest irritation is obtained by watery suspensions, for instance, in mucilage. Olive oil and turpentine produce practically no hyperemia; ether and absolute alcohol produce very little hyperemia; 95 per cent. alcohol causes a distinct hyperemia, whereas 50 per cent. alcohol causes marked and lasting hyperemia; mucilage of acacia and simple syrup cause the most intense and persistent hyperemia. (T. Sollman, *Journal of Pharmacology and Experimental Therapeutics*, through the *Journal of the American Medical Association.*)

PHARMACOLOGIC STUDY OF BENZYL ALCOHOL.—Experimental data and clinical cases show that benzyl alcohol is an efficient local anesthetic when administered in aqueous solution. This alcohol is soluble up to 4 per cent. in water or in physiologic saline solution. These concentrations appear to be entirely efficient for practical purposes. The interesting features in connection with this drug which should be especially emphasized are in the first place its low toxicity

as compared with that of the commonly employed local anesthetic alkaloids of which cocaine is the standard representative. The next interesting and important feature in connection with benzyl alcohol as an anesthetic is the ability of the organism to metabolize it and excrete it in an innocuous form. Third, an important feature of this local anesthetic is its high boiling point and the consequent ease of sterilization. Last, the comparatively low price of the drug and its ease of production. (D. I. Macht, *Journal of Pharmacology and Experimental Therapeutics,* April, 1918, through the *Journal of the American Medical Association.*)

ACRIFLAVINE AND PROFLAVINE.—An investigation was undertaken by Carslaw and Templeton with the object of ascertaining whether the action of proflavine differed in any way from that of acriflavine. Since October, 1917, a large proportion of the infected gunshot wounds admitted to one hospital have been treated with acriflavine, and the clinical results have been observed in over sixty cases. Proflavine followed by eusol was used in thirty cases (thirty-two wounds being treated). In all cases 1 : 2,000 solution in normal saline was used. The rapid improvement in the general condition of patients as shown by subsidence of temperature, pulse rate, etc., and rapid disappearance of pain and of inflammatory edema in the vicinity of wounds were very evident. Although the action of acriflavine and proflavine is very similar there can be no doubt that proflavine is slower. The improvement in the general condition of patients is not so rapid. The formation of the fibrinous membrane is not usually complete until the fifth, sixth, or seventh day in contrast with its presence on the third, fourth, or fifth day when acriflavine is used. Further, separation of membrane and attainment of a "clean" wound are also slightly delayed. The application of flavine to affected wounds does not render them bacteriologically sterile. Flavine is clearly antiseptic, not disinfectant in action. There is a complete absence of evidence of damage to tissues when these salts are used in solution not stronger than 1 : 1,000. There is no necrosis of any of the exposed tissues. These salts are of undoubted value in controlling and preventing the spread of sepsis, as is shown by the rapid improvement in local and general conditions. This object having been gained, there is no advantage in continuing their use, as a condition is used in which reparative changes are

slow, although not by any means absent. Following on the substitution, after a few days, of a more stimulating antiseptic, for instance, eusol, a "clean" wound is obtained sooner than by any other form of treatment known to the authors. There is no evidence of any general toxic effect. (*The Lancet,* through the *Journal of the American Medical Association.*)

Brilliant Green and Gunshot Wounds.—Of a large number of cases treated with brilliant green information regarding their subsequent progress was obtained in only forty-six cases. The wounds had, without exception, been received from two to eight hours previous to treatment, and were all severe, with considerable tissue damage. No special type of case was selected, but it was not used in cases involving the peritoneal or pleural cavities, though there seems to be no reason why it should not be used. The solutions used were: (1) 1:1,000 brilliant green in normal saline; (2) 1:500 in normal saline; (3) 1:500 in 0.5 per cent. chloretone. Of the solutions No. 3 was preferred. It appeared to have a definitely analgesic effect, rendering dressing less painful. Wounds appear to clean more quickly under the stronger solutions. No toxic symptoms were observed in any case. Results were recorded by independent observers and reported, for the most part, by means of Form M. R. C. 1, since it was necessary to evacuate early. When possible a complete excision of damaged tissue was carried out and foreign bodies were removed. In cases of compound fracture all fragments of bone having no periosteal attachment were removed. Damaged tissue is more deeply stained by brilliant green than is healthy tissue. It is useful in this respect when excising the tracks of missiles. All tissue, except skin, which holds the stain of 1:500 solution, should be excised. Brilliant green produces exuberant, but very vascular, bright red granulation. Noticeable features in cases treated with it are the absence of edema and the inflammation round the wound and the rapidity with which sloughs and sequestra separate. It is painless in application and does not appear to interfere with the growth of epithelium. For these reasons it may be considered a useful antiseptic, and though it can by no means atone for an incomplete or faulty primary excision it may be used with advantage where anatonic conditions render complete primary excision impossible. (*The Lancet,* through the *Journal of the American Medical Association.*)

HYPOCHLORITE AND CHLORAMIN-T SOLUTION.—Exact determinations of the rapidity of the fall in chlorine concentration on pathologic and on normal skin under experimental conditions, were made by Austin and Taylor because they might be of value to surgeons using Dakin's hypochlorite and chloramin-T solutions clinically. The left ears of three white rabbits of the same relative size and weight were exposed to the rays emitted by a Coolidge tube. The spark gap used measured three inches; the miliamperage was 110; the distance from the target to the ear was six inches; and the time of exposure was twenty minutes. Eight weeks later the roentgen rayed ears each exhibited a sharply demarcated gangrenous area over which there was considerable crusting of epithelium and secretions and in the lumen there was much thick pus. The ears of the affected rabbits were each suspended for twenty minutes in a beaker containing 400 Cc. of the solution to be tested.

The fall in chlorine concentration of Dakin's hypochlorite solution was more rapid in contact with necrotic than in contact with normal tissue. The fall in chlorine concentration of chloramin-T solution was very slight when applied to necrotic tissue and is negligible when applied to normal tissue. The action of the hypochlorite solution on tissue resulted in the separation of particles of necrotic tissue, hair, epithelial scales, coagulated serum, etc., and a gradual digestion of these substances, taking place over a period of at least seventeen hours. The fall in the chlorine concentration of hypochlorite solution was not complete until the particles were completely dissolved. Chloramin-T solution, 2 per cent., had no erosive effect comparable with that exhibited by the hypochlorite solution. Repeated exposure to the three solutions showed that the hypochlorite solution was superior in its cleansing ability on necrotic tissue. The hypochlorite solution was much more irritating to normal rabbit skin than chloramin-T solution or the alkaline control solution. Therefore, the authors conclude that irritating effects must be due to the readily available chlorine. (From the *Journal of Experimental Medicine,* through the *Journal of the American Medical Association.*)

TOXICITY OF CERTAIN ANTISEPTICS.—The toxic action of a number of antiseptic substances in common use was investigated by Taylor and Austin. The method was to inject increasing doses into

mice intraperitoneally and into guinea-pigs both subcutaneously and intraperitoneally. The only antiseptic of which the smallest fatal dose was smaller than the largest survival dose was dichloramin-T. Since two mice survived 4.7 Mg. per 100 Gm. of body weight, it is probable that 15.5 Mg. rather than 1.6 Mg. is to be considered the smallest fatal dose for this series. Of all the substances tested, eucalyptol and brilliant green were the most toxic, the lethal dose of each being 0.1 Mg. per 100 Mg. of body weight. Mercurophen, mercuric chlorid, and chloramin-T constitute the group with the next highest toxicity, the lethal dose being 1 Mg. per 100 Gm. of body weight. Dichloramin-T, proflavine and the four hypochlorite solutions tested follow in the order named with a lethal dose of about 10 to 15 Mg. per 100 Gm. of body weight. The least toxic chemicals are iodine and phenol, of which the lethal doses are about 50 Mg. per 100 Gm. of body weight. The lethal dose of Dakin's hypochlorite solution injected under the skin of the abdomen of guinea-pigs per 100 Gm. of body weight is the same as that determined intraperitoneally in the mouse. Chloramin-T and dichloramin-T administered in this manner gave rise to local necrosis with extensive sloughing. Therefore, the substances injected intraperitoneally into mice and guinea-pigs arranged in the order of their decreasing toxicity are: eucalyptol and brilliant green; dichloramin-T and proflavine; hypochlorite, Dakin's hypochlorite, Javelle water, and magnesium hypochlorite, iodine, and phenol. Now that Dakin's bland solvent, chlorcosane, is available as a vehicle for dichloramin-T, the authors advise that eucalyptol should be discarded for this purpose because of its much greater toxicity. (From the *Journal of Experimental Medicine,* through the *Journal of the American Medical Association.*)

Report on Carrel-Dakin Solution.—Contrary to many observers the authors believe that the Carrel technic is not a complicated one. It requires no more time, labor or material than the method of treating purulent collections with drainage tubes and irrigations of saline, mercuric bichloride or phenol solutions. The deodorizing effect of this solution is very important. This has a psychologic effect in aiding the patients' convalescence. The irritating effect of the solution on skin surfaces has been very slight. The authors have abandoned the use of gauze strips saturated with

petrolatum and use no protection at all, except when the skin appears hypersensitive, in which case a spray of liquid paraffin is used. The mucous surfaces appear to suffer no more than the skin, as instanced by the use of the solution as a vaginal douche.

Emphasis is laid on the contraindication to the use of the solution in cases in which there is much hemorrhage. This is controlled as well as possible at time of operation and the solution not used until twenty-four to forty-eight hours have elapsed. Other contraindications to the use of the solution are in infections due to the *Bacillus pyocyaneus,* on which it seems to have no effect, and in all classes of wounds after the infection has been controlled, when it is unnecessary and has a retarding influence on granulations. In fecal fistulas the solution is not used, because it has been noticed that patients with this condition suffer with a great deal of discomfort, and at times pain, for three to four hours after the dressing.—(Drs. J. B. Deaver, Lankenau Hospital, Philadelphia, J. W. Bodley, W. H. Means and H. E. Knox, Philadelphia. From the *Medical Record,* New York, through the *Journal of the American Medical Association.*)

RINGWORM OF THE SCALP.—Douglas Freshwater gives several useful prescriptions for ringworm of the scalp. In small families, to prevent the other children becoming infected, it is a safe plan to dress the hair daily with the following brilliantine:

| | | |
|---|---|---|
| ℞ | Acid salicylic | gr. x |
| | Ol. lavand. | ♏ v |
| | Ol. bergam. | ♏ v |
| | Ol. olivæ | ad ℥i |

A useful antiseptic shampoo wash is:

| | | |
|---|---|---|
| ℞ | Thymol | gr. xv |
| | Sap. mollis | ℥i |
| | Sp. vin. rect. | ℥i |

This is allowed to remain some 10 or 15 minutes on the scalp before being rinsed off.

Oleate of copper is useful before and during the period of epilation:

| | | |
|---|---|---|
| ℞ | Cupri oleatis | ℥i |
| | Hydrarg. oleatis | gr. xxv |
| | Adipis lanæ hydros. | ℥i |
| | Ol. olivæ | ℥i |

William's picric acid lotion is as follows:

| | | |
|---|---|---|
| ℞ | Camphor | ʒiv |
| | Sp. vin. rect. | ʒvi |
| | Acid picric | gr. viii |

Solve. Sig.—"Inflammable. To be painted over the scalp twice daily." Generally the ringworm hairs are loosened, and come away with their bulbous portions in from ten to thirty days. A yellow staining of the hair may be noticeable some weeks after treatment. From *The Prescriber,* September, 1918.

## TRADE INTEREST.

To Manufacture Coconut and Palm Oil in Colon.—An American company with a capital of $50,000 is constructing at Colon a two-story concrete building for manufacturing coconut and palm oils, soap, and their by-products, glycerin, caustic potash, carbonate of potash, soda, etc. It will be possible to make 1,500 gallons of coconut oil and 250 gallons of palm oil daily. The factory will also have a daily capacity to manufacture 500 boxes (60 pounds each) of laundry and toilet soaps. The company has two schooners for trading along the coast and bringing coconuts to the factory; and as coconuts were exported from Colon in 1917 to the number of 19,528,843, an ample supply of these nuts can be obtained for the factory the year round. Palm oil will be extracted from the nuts of the Guinea, Coroza Grande, and other palm trees growing in various parts of the Republic of Panama, as well as in the Canal Zone. It is proposed to make other vegetable oils, but in limited quantities. As the manager of this oil factory has had much experience in such work, and as the supply of raw material is ample and the demand for vegetable oils large, the new company should be quite successful in its operations in Colon. (The address of the company can be obtained from the Bureau of Foreign and Domestic Commerce or its district or coöperative offices by referring to file No. 104,987.) (Consul Julius D. Dreher, Colon, from "*Commerce Reports,*" August 22, 1918.)

Control of Camphor Production in Taiwan.—Seven officials and experts are being appointed by the Monopoly Bureau in the Japanese Government General of Taiwan (Formosa). They will undertake the control of camphor production and will conduct in-

vestigations into the camphor market. This step has been taken to prevent the decay of the camphor industry in Taiwan in view of the probable decrease in production this year of about 1,000,000 pounds. (From *Weekly Bulletin,* Canadian Department of Trade and Commerce, Ottawa, August 5, through *Commerce Reports,* August 22, 1918.)

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## BOOK REVIEWS.

A TEXT-BOOK OF CHEMISTRY INTENDED FOR THE USE OF PHARMACEUTICAL AND MEDICAL STUDENTS. By SAMUEL P. SADTLER, Ph.D., LL.D., VIRGIL COBLENTZ, Ph.D., F.C.S., and JEANNOT HOSTMAN, Ph.G. Fifth Edition, Revised and Rewritten. Philadelphia and London, J. B. Lippincott Company.

We are pleased to note the appearance of the fifth edition of this approved text-book of chemistry for the use of pharmacy and medical students. Throughout this revision bears testimony to the thoughtfulness and care that has been exercised by the authors in the selection from the broad field of general chemistry of those subjects that relate especially to materia medica and the duties of the closely allied professions of medicine and pharmacy in the discharge of their service to their fellowmen. The changes effected by the Ninth Decennial Revision of the Pharmacopœia and likewise the newer remedies have been incorporated in the revised text.

The experience of the authors as teachers is evidenced by the concise, yet clear, methods adopted for the presentation of the numerous rather intricate subjects necessarily included in a text-book of this character and purpose. The scope of the work, while limited to the needs of students of the professions it is intended to serve, nevertheless, presents the subjects of general chemistry and the physics related thereto, sufficiently in detail to serve as the foundation for future higher study in special fields of analytical and research work.

The typography, printing and binding are excellent and the illustrations, while not profuse, are sufficient and very well demonstrate the theories, facts and methods shown.

The contents of the book are presented in four divisions of the subject matter, Part I being devoted to the consideration of Ele-

mentary Physics, Part II to Chemistry of the Non-Mentals, Part III to Chemistry of the Metals and Part IV to Organic Chemistry.

It is noted that the classification of the elements and the periodic system is treated in Chapter VIII of Part II after six preceding chapters of this part have discussed the history, physical and chemical properties and uses of the non-metal elements. A more logical place for the presentation of this subject would appear to be in association with the "theoretical introduction" given in Chapter I. Likewise the treatment of "Electrolysis and Its Application" as Chapter XII of Part IV, Organic Chemistry, would appear as somewhat incongruous. These minor criticisms, however, do not detract from the accuracy of the information given and the value of the work as a most acceptable handbook alike for the average physician and pharmacist as for the students who are preparing for life work in these callings.

G. M. B.

AMERICAN DRUG MANUFACTURERS ASSOCIATION PROCEEDINGS FOR NINETEEN HUNDRED AND EIGHTEEN.

It has been quite a treat to peruse this volume of 343 pages detailing the proceedings of the "Seventh Annual Meeting of the American Drug Manufacturers Association, held at the Waldorf-Astoria Hotel, New York City, January 28–30, 1918. The addresses, papers, reports and discussions bear throughout the evidence of a very live association whose members are familiar with the national, trade and scientific problems associated with the manufacture of medicinal preparations and are energetically meeting these with the ability of well-equipped modern business men.

The reports of the various committees deal not only with the internal affairs that are the special problems of this association, but, likewise, consider many questions that are of general import to all manufacturers and merchants. Not the least important is the report of the Committee on Standards and Deteriorations. It is apparent that the membership of the association of drug manufacturers will give to this committee of the organization exceptional facilities for a most valuable piece of constructive work in the determining of proper standards for drugs and the rates of deterioration of medicines of a non-permanent character. Their coöperation with the various committees of revision of the legal standards and the govern-

mental departments and other scientific and technical organizations which are likewise interested in these problems, will doubtless prove of great value.

The secretarial and editorial work of the book is fully in keeping with the high class of its contents. What is equally evident throughout the "Proceedings" is the prospects for the continuation of the many good works that have been so auspiciously inaugurated. We extend our hearty congratulations and shall anticipate the pleasure of noting many more yearly proceedings indicative of the same spirit and progress shown in the present volume.

G. M. B.

A Critical Revision of the Genus Eucalyptus. By J. H. Maiden, I.S.O., F.R.S., F.L.S., Government Botanist of New South Wales and Director of the Botanic Gardens, Sydney. Vol. IV, Part 5.

It has been our privilege to note from time to time in these pages, the appearance of the parts of this elaborate monographic study of the Eucalypti. The Part XXXV of the complete work, that is now in hand, deals in the approved style adopted for this monograph with the following species: *Eucalpytus Lehmanni* Preiss., *E. annulata* Benth., *E. platypus* Hooker., *E. spathulata* Hooker., *E. gamophylla* F. v. M., *E. argillacea* W. V. Fitzgerald.

The four lithographic plates illustrating the text of this part are of the same excellent quality as has been shown throughout the monograph.

G. M. B.

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## OBITUARY.

### JOHN C. GALLAGHER.

When John C. Gallagher died in Jersey City on October 2, 1918, the retail drug trade lost one of its most enthusiastic and efficient workers.

The deceased was born in Brooklyn, November 4, 1861. After attending the public schools and St. John's College in Brooklyn he entered the employ of T. C. Prevost. He was a member of the class of 1882 in the College of Pharmacy of the City of New York.

In 1882 he came to Jersey City as junior clerk in the store of Evan C. Kennedy at the corner of Grove and Seventh Streets. In rapid succession he advanced to senior clerk, manager and proprietor. He continued in the latter capacity until illness compelled his retirement a short time before his death.

Mr. Gallagher became a member of the N. A. R. D. in the very beginning of its existence. During the crucial times of its formative period he was always one of the leaders whose advice was treasured by his fellow workers. In 1893 he joined the American Pharmaceutical Association and in 1894 he became a member of the College of Pharmacy of the City of New York becoming a life member in 1914. He was a most enthusiastic member of the Jersey City Retail Druggists Association of which he was an ex-president as well as one of the founders. Mr. Gallagher was elected a member of The New Jersey Pharmaceutical Association in 1899 and in 1915 he was elected to life-membership by the association in recognition of his untiring efforts during his term as president which had just expired.

"John C." as his friends and admirers, who were legion, called him, was ever a power for good in organized pharmacy. Wherever anything concerning his profession, either professionally or commercially, came up he was on the spot and with loyalty and devotion and with untiring energy he brought to bear the influence born of clear head and far-sightedness. Legislative work attracted him and in this field he was at his best. Many a suggested statute was changed for the benefit of pharmacy due to his work with the lawmakers. Some called him a politician. This was not so. He was simply an earnest worker devoted to his chosen profession, ever willing to do much more than his share to make its environments better, who knew how to properly present the questions under debate to those who were not pharmacists. Would that there were many more like him! His loss to organized pharmacy will be a lasting one. His work in The New Jersey Pharmaceutical Association has become a matter of history.

He is survived by his widow, Della C. Gallagher, and one daughter, Hazel.

The funeral took place on the morning of October 4, 1918, from St. Michael's Church, Jersey City.

JEANNOT HOSTMANN.

# INDEX TO VOLUME 90 OF THE AMERICAN JOURNAL OF PHARMACY.

## AUTHORS.

SUBJECTS.

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